

A Multi-Dimensional Psychiatric Perspective on the Impact of the COVID-19 Pandemic

Cana Aksoy Poyraz¹ , Ömer Faruk Demirel¹ , Burç Çağrı Poyraz¹ , Serdar M. Dursun² 

¹Department of Psychiatry, Istanbul University- Cerrahpaşa School of Medicine, Istanbul, Turkey; ²Department of Psychiatry, University of Alberta, Canada

ABSTRACT

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) arose in Wuhan, China in December 2019 and spread worldwide rapidly, and was declared a global pandemic by the World Health Organization as of March 2020. As the SARS-CoV-2 pandemic has spread worldwide, its impact is increasingly being recognized among vulnerable groups and also by the public in general. Recent findings indicate that patients with mental health disorders are among the groups most vulnerable to psychological stress and social hardships related to the current pandemic. Studies also indicate an increased risk of infection by SARS-CoV-2 in subjects with psychiatric disorders. Patients affected by SARS-CoV-2 may present to the psychiatrist with delirium, psychotic symptoms, depression, anxiety, post-traumatic stress disorder, and insomnia. Some patients will develop persistent somatic symptoms such as fatigue after the acute infection. In this article, we summarize the preliminary findings related to the effects of the SARS-CoV-2 pandemic on patients with mental health disorders, as well as recent research on psychiatric presentations in patients affected by SARS-CoV-2.

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INTRODUCTION

Since the beginning of the SARS-CoV-2 pandemic, the effects of the pandemic on mental health and on patients with existing mental illness have been a challenging concern globally. Preliminary research indicates that patients who recovered from SARS-CoV-2 infection appear to be at increased risk of psychiatric disorders, and patients with mental illness are more susceptible to SARS-CoV-2 infection. Moreover, a less favorable prognosis related to SARS-CoV-2 infection has been reported in individuals with severe mental disorders.¹⁻⁴ In this article, we summarize the preliminary findings related to the effects of the SARS-CoV-2 pandemic on patients with mental health disorders, as well as discuss the recent research on psychiatric presentations in patients affected by SARS-CoV-2.

Impact of the COVID 19 Pandemic on Patients with Psychiatric Disorders

Patients with mental health disorders are among the groups most vulnerable to the effects of the coronavirus 2019 (SARS-CoV-2) pandemic for several reasons. Firstly, many risk factors associated with psychiatric disorders, such as poor self-control, lack of insight, poor self-care, reduced awareness of risks, and socioeconomic disadvantages, may predispose individuals with pre-existing psychiatric

disorders to SARS-CoV-2 infection. To support this hypothesis, recent studies indicate an increased risk of SARS-CoV-2 infection in subjects with psychiatric disorders.^{1,2} Also, once SARS-CoV-2 is contracted, it may be more difficult for them to access testing and treatment on time, and discrimination associated with mental illness may aggravate this problem.⁵ Indeed, 2 cohort studies have found that a diagnosis of schizophrenia was associated with an increased risk of death after SARS-CoV-2 infection.^{3,4} Finally, people with pre-existing psychiatric disorders may be prone to relapses or worsening of their existing psychiatric conditions due to stressors and hardships of the SARS-CoV-2 pandemic such as the perceived threat posed by the pandemic, extensive home-confinement directives, general misinformation, a worsening economic situation, and/or limited access to routine psychiatric care.⁵

In Turkey, the first confirmed SARS-CoV-2 case was identified in March 2020, and since then, numerous regulations from the government have come into effect. During the first wave of the pandemic (March-June 2020), hospitals reduced the number of daily admissions in outpatient and inpatient clinics, and psychiatry clinics were profoundly affected by these changes. Several psychiatric inpatient wards were closed or operated at decreased capacity, and administration of Electroconvulsive therapy was interrupted. During this period, to ensure the continuation

Corresponding author: Cana Aksoy Poyraz, E-mail: aksoycana@gmail.com

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of psychiatric care for our existing patients, we informed our patients and their care-givers of a telepsychiatry service that we started for those whose access to our psychiatry department has severely limited the pandemic. In parallel, we investigated the effects of the SARS-CoV-2 outbreak and public health measures on the psychological well-being of outpatients with psychiatric disorders. In a survey of 436 outpatients being seen in the Cerrahpaşa psychiatry clinics, we found that patients with psychiatric disorders reported a high rate of psychological distress as an immediate response to the SARS-CoV-2 outbreak. Notably, approximately one-third of the patients in our study met the 'probable' diagnosis of post-traumatic stress disorder (PTSD), with over 80% of these subjects reporting comorbid depression. In addition, over one-fifth of the patients felt that their psychological status worsened considerably during the SARS-CoV-2 outbreak. A significant proportion of our patients (46.3%) reported that they had recently been avoiding outpatient visits because of the fear of contracting the infection. Interestingly, avoiding outpatient visits because of the fear of infection was significantly related to high psychological distress. Among the psychiatric conditions, unipolar depression and anxiety spectrum disorders were significantly associated with high levels of PTSD symptoms. Conversely, the diagnoses of schizophrenia, and to a much smaller extent, bipolar disorder, were related to lower severity of PTSD symptoms.⁶ During the first wave of the pandemic (March-June 2020), other research conducted on the effects of SARS-CoV-2 in psychiatric patients yielded fairly similar results. In the first study from China, Hao et al. compared the severity of symptoms of PTSD, anxiety, and depression between psychiatric outpatients ($N = 76$) and healthy controls, and found a greater psychological impact of the outbreak in the former group; notably, 31% of the patients in the study had a 'probable' diagnosis of PTSD in contrast to only 13.8% of the controls.⁷ Another online study with a large sample size ($N = 2065$) from Chengdu, China, found that around a quarter of existing psychiatric outpatients had clinically significant anxiety and insomnia, and 1 in 6 patients had depression.⁸ The psychological distress reported in this Chengdu study was lower than what we found in our studies. This was probably due to the timing of their study, which

coincided with the end of the pandemic in that country. The authors also found that 20.9% of patients reported a deterioration of their mental health condition due to the restrictions linked to the pandemic. Patients with transportation restrictions, isolation at home, and fear of cross-infection in hospitals were particularly susceptible to such deterioration. The survey also found that a quarter of new-onset cases, including those with anxiety, depression, insomnia, and psychosis, could not receive timely diagnosis and treatment. Similarly, around a quarter of the existing patients diagnosed with mental disorders, including depression, bipolar disorders, and schizophrenia, could not receive routine psychiatric care because of suspended hospital visits.⁸ Another study investigating 205 patients with serious mental illness in Italy found that subjects had significantly higher levels of stress, anxiety, and depression at the peak of the outbreak than healthy controls.⁹ The authors found that patients were 4 times more likely to perceive high SARS-CoV-2 pandemic-related stress, and had a 2- to 3-fold greater risk of developing severe anxiety and depressive symptoms, which suggested that the level of distress related to the SARS-CoV-2 pandemic perceived by patients with serious mental illness was markedly higher than that perceived by the general population.⁹

Psychiatric Pharmacotherapy and SARS-CoV-2

A recent meta-analysis¹⁰ showed that antidepressant treatment, including treatment with the selective serotonin reuptake inhibitors (SSRIs), was associated with decreased plasma levels of pro-inflammatory mediators. High plasma levels of inflammatory mediators, including cytokines and chemokines, were associated with increased SARS-CoV-2 severity¹¹ and mortality.^{11,12} In a recent observational multi-center retrospective cohort study conducted in France, Hoertel et al. found that receiving any antidepressant within the first 48 h of hospital admission was associated with a lower risk of death or intubation in patients hospitalized for SARS-CoV-2 infection.¹³ Several mechanisms were suggested to explain the probable protective effects of antidepressant use in SARS-CoV-2 infection. Antidepressants that functionally block acid sphingomyelinase activity can prevent the infection of epithelial cells via SARS-CoV-2 in vitro.¹⁴ Another potential mechanism for the antidepressants' immune-modulatory effects is through σ -1 receptor (S1R) agonism.¹⁵ Various antidepressants are S1R agonists,¹⁶ and therefore, they might potentially prevent the cytokine storm observed in severe COVID-19.¹⁷ In a recent randomized trial of adult outpatients with symptomatic SARS-CoV-2, patients treated with fluvoxamine (an SSRI, an S1R agonist, and a functional inhibitor of acid sphingomyelinase activity) were compared with patients on placebo, and the fluvoxamine-treated patients had a lower likelihood of clinical deterioration over 15 days.¹⁶ Also, certain antidepressants such as fluoxetine may exert antiviral effects on SARS-CoV-2.¹⁸ Larger randomized trials will be

MAIN POINTS

- There is an increased risk of SARS-CoV-2 infection in subjects with psychiatric disorders.
- We have summarized the preliminary findings related to the effects of the SARS-CoV-2 pandemic on patients with mental health disorders.
- Significant symptoms of post-traumatic stress, anxiety, and depression were found in patients affected by SARS-CoV-2 infection.
- Long-term follow-up studies will reveal the psychiatric morbidity in patients recovered from SARS-CoV-2 infection.

needed to determine the clinical efficacy of antidepressant medications on SARS-CoV-2.

Conclusion

These findings call for the need to develop specialized public policies which focus on individuals with mental health problems and which aim to protect them against the infection and hardships related to the pandemic. Public health policy-makers should consider an early vaccination program for individuals with severe mental disorders such as schizophrenia, for whom a less favorable prognosis related to SARS-CoV-2 infection has been reported. Mental health policies should adopt a proactive stance, which can facilitate early recognition of deterioration in patients' mental health status. Alternative methods such as telepsychiatry can be utilized in order to ease the trauma caused by reduced access to mental health services.

Psychiatric Disorders in Patients Affected by SARS-CoV-2 Infection

Patients with SARS-CoV-2 infection may present with delirium, insomnia, depressed mood, anxiety, and/or PTSD symptoms in the acute and immediate convalescent period (Table 1). Delirium can be a presenting symptom in SARS-CoV-2 or can develop during the course of the disease. A recent multi-center cohort study ($N = 817$) indicates that around 28% of older SARS-CoV-2 patients had delirium at presentation to the emergency department, and around one-third of these subjects did not have the typical SARS-CoV-2 symptoms such as fever or shortness of breath.¹⁹ The prevalence of delirium increases with greater disease severity, such that as high as 55% of the critical patients with SARS-CoV-2 infection in intensive care units (ICUs) experience delirium, according to a large multi-center cohort study ($N = 2088$).²⁰ Delirium in the context of SARS-CoV-2 has been associated with worse outcomes (ICU-stay, mechanical ventilation, and death).^{19,21} Other potential complications are prolonged delirium and/or dementia, which can be detected in a substantial proportion of these patients after discharge.²²

Anxiety, depressed mood, PTSD symptoms, and insomnia are commonly reported in patients during acute infection with SARS-CoV-2. A large data set of SARS-CoV-2-infected individuals ($N = 40,469$) showed that neuropsychiatric manifestations were frequent (22.5%), and that the common psychiatric manifestations were anxiety (4.6%), mood disorders (3.8%), insomnia (3.4%), and other symptoms of emotional state (0.8%).²³ Studies that specifically investigated acutely hospitalized SARS-CoV-2 patients using self-reporting measures reported comparatively higher frequencies of clinically significant emotional symptoms,²⁴⁻²⁷ with a prevalence as high as 96% in 1 report.²⁷ Several risk factors were associated with increased emotional disturbances during the acute infection; these included being female, prior psychiatric

disorder, staying alone in a hospital room, being in the early days of hospital stay, decreased oxygen saturation levels, and a family infection with SARS-CoV-2.^{24,28}

Cases of first-episode psychosis and mania in people infected with SARS-CoV-2 have been reported.²⁹⁻³² In a recent study, Brown et al. (2020) undertook a review of data related to previous viral outbreaks (SARS and MERS), and reported that the incidence of psychotic symptoms in people infected with the virus was between 0.9% and 4%, based on 4 observational studies.³³ However, the etiology seems complex, and it is necessary to consider factors such as potential viral effects on the CNS, the stress related to the pandemic, and/or treatment with the use of corticosteroids, antivirals, or hydroxychloroquine.²⁹ Another problem is the differentiation of the psychosis from delirium-related psychotic symptoms. A recent study based on a large electronic record system from the US found that survivors of SARS-CoV-2 infection were at increased risk for a new diagnosis of anxiety and a mood disorder, dementia, or insomnia, as well as psychosis, in the 6 months after the diagnosis.³⁴

The neuropsychiatric conditions observed in SARS-CoV-2 can be multifactorial. Potential mechanisms are the direct viral invasion of the brain, causing encephalitis, neuroinflammation, peripheral organ dysfunction, and cerebrovascular changes, acting separately or together to cause neuropsychiatric symptoms.³⁵ The SARS-CoV-2 virus can also affect the CNS by producing a cytokine storm.³⁶ Alternatively, chronic low-grade inflammation has also been proposed to be associated with neuropsychiatric manifestations.³⁶ To date, various biological alterations associated with SARS-CoV-2 have been identified, and some of them, especially those related to the activation of microglia and cytokine signaling, might be of relevance to specific mental health outcomes.³⁷ Other factors that should be considered are the psychological trauma related to being diagnosed with a potentially fatal disease, hospitalization/isolation, medical treatments, stigma, and the SARS-CoV-2 pandemic.

Potential long-term psychiatric consequences of SARS-CoV-2 infection are worrisome. Previously, most patients recovered without experiencing acute mental illness during the SARS and MERS epidemics.³⁸ However, in some patients, symptoms of PTSD, depression, and/or fatigue were present and persistent, with significant distress and impairment in psychosocial functioning even after many years. Similarly, or possibly to a greater extent, depression, anxiety, fatigue, and PTSD may continue to be important concerns in a subgroup of patients after the current SARS-CoV-2 pandemic. Recent studies investigating the psychiatric symptomatology in patients who have recovered from acute SARS-CoV-2 infection reported high rates of insomnia and symptoms of PTSD, depression, and anxiety about 1 month after the infection.³⁹⁻⁴¹ Mazza et al. reported that more than half of their subjects with

Table 1. Studies Concerning Psychiatric Symptoms in Patients Recovered from SARS-CoV-2 Included in the Review

	Country	Design	Sample	Measures	Results
Kennedy et al. ¹⁹ 2020	USA	Cohort study	817 older adults (aged >65 years old) presented to the Emergency Department	medical records review	Delirium 28%
Pun et al. ²⁰ 2021	14 countries	Multi-centre cohort study	2088 patients admitted to ICUs	electronic health records review	Delirium 54.9%
Ragheb et al. ²² 2020	USA	Case series	148 patients discharged from ICUs	retrospective chart review	Delirium 24% Cognitive impairment 23% Depression 12%
Garcez et al. ²¹ 2020	Brazil	reviews of electronic medical records	707 patients, >50 years, admitted to the hospital	Chart-Based Delirium Identification Instrument (CHART-DEL)	Delirium 33%
Nalleballe et al. ²³ 2020	USA	reviews of real-time electronic medical records	40469 patients	Electronic medical record analysis	Neuropsychiatric symptoms 22.5% Anxiety 4.6% Mood disorders 3.8% Suicidal ideation 0.2%
Şahan et al. ²⁴ 2021	Turkey	Cross-sectional	281 patients hospitalized with SARS-CoV-2	Hospital Anxiety and Depression Scale (HADS)	Anxiety 34.9% Depression 42%
Paz et al. ²⁵ 2020	Ecuador	Cross-sectional	759 individuals (40.3% confirmed, 59.7% suspected cases)	Patient Health Questionnaire (PHQ-9) Generalized Anxiety Disorder (GAD-7)	Depression 29.2% Anxiety 24.2%
Zandifar et al. ²⁶ 2020	Iran	Cross-sectional	106 inpatients with SARS-CoV-2	Depression, Anxiety and Stress Scales-21 (DASS-21) Perceived Stress Scale (PSS-4)	Depression 97.2% Anxiety 100%
Tomasoni et al. ⁴¹ 2021	Italy	Cross-sectional	105 Patients with SARS-CoV-2	Hospital Anxiety and Depression Scale (HADS-A/D)	Pathological HADS-A/D 30% persistent symptoms 52.4%
Mazza et al. ⁴⁰ 2020	Italy	Cross-sectional	402 adults surviving COVID-19 (1 month after discharge)	Impact of Events Scale-Revised (IES-R) PTSD Checklist for DSM-5 (PCL-5) Zung Self-Rating Depression Scale (ZSDS) Beck's Depression Inventory (BDI-13) State-Trait Anxiety Inventory form Y (STAI-Y) Medical Outcomes Study Sleep Scale (MOS-SS) Women's Health Initiative Insomnia Rating Scale (WHIIRS) Obsessive-Compulsive Inventory (OCI)	PTSD 28%, depression 31% anxiety 42% Obsessive-Compulsive symptoms 20%, Insomnia 40%
Bo et al. ²⁷ 2020	China	Cross-sectional (online survey)	714 SARS-CoV-2 recovered patients prior discharge	PTSD Checklist (PCL-C)	PTSD 96%
Poyraz et al. ⁴² 2021	Turkey	Cross-sectional (online survey)	284 patients diagnosed with SARS-CoV-2 (50 days following diagnosis)	Impact of Events Scale-Revised (IES-R) Hospital Anxiety and Depression Scale (HADS), Pittsburgh Sleep Quality Index (PSQI)	PTSD 25.4% Anxiety 18.4% Depression 18.8% Poor sleep 38.8%
Kong et al. ²⁸ 2020	China	Cross-sectional	144 patients diagnosed with SARS-CoV-2	Hospital Anxiety and Depression Scale (HADS) Perceived Social Support Scale (PSSS)	Anxiety 34.72% Depression 28.47%

Liu et al. ³⁹ 2020	China	A cross-sectional survey	675 patients discharged from hospital	Generalized Anxiety Disorder scale (GAD-7) Patient Health Questionnaire (PHQ-9) PTSD Checklist for DSM-5 (PCL-5)	PTSD 12.4% Anxiety 42.7% Depression 65.7%
Varatharaj et al. ³² 2020	UK	Nationwide, cross-specialty surveillance study	125 patients diagnosed with SARS-CoV-2	Online network of secure rapid-response case report notification portals	Altered mental status 31%

PTSD, post-traumatic stress disorder; ICU, intensive care units.

prior SARS-CoV-2 infection had clinically significant anxiety, depression, PTSD, and/or obsessive-compulsive symptoms at about 1-month follow-up after the hospital treatment.⁴⁰ Similarly, Liu et al. found that “moderate-to-severe” depression and anxiety were present at around 10% and 20%, respectively, after about 1 month following hospital discharge. In this study, the prevalence of significant PTSD was 12%.³⁹ In another study, one-third of the patients with SARS-CoV-2 infection reported clinically significant anxiety and/or depression, at a median of 46 days after virus clearance.⁴¹ We recently performed a cross-sectional survey study investigating the psychological well-being of patients with a diagnosis of SARS-CoV-2 infection, after completion of their initial medical care at the Cerrahpaşa Medical Faculty. We found that after a mean time period of almost 50 days following the diagnosis, 34.5% of subjects reported clinically significant PTSD, anxiety, and/or depression, with PTSD being the most common condition reported (25.4%). In our survey, female gender and psychosocial factors such as prior traumatic experiences, stigmatization, and perceived threat related to the ongoing pandemic were associated with the PTSD risk, rather than medical factors such as infection severity, very low pulse oxymetry readings, or the need for supplemental oxygen.⁴² There may be a chronic low-grade inflammation, or other immunological alterations, which may potentially impact the development of medium- and long-term symptoms following the acute infection.³⁶

A significant proportion of SARS-CoV-2 patients continues to experience persistent somatic symptoms such as fatigue, breathlessness, difficulty in concentration, and sleep problems which may cause significant disability.⁴²⁻⁴⁴ Although the etiology of the persistence of such symptoms is not clear and is probably heterogenous, similar symptoms were reported after the onset of previous viral pandemics. For instance, in the follow-up of SARS survivors, chronic fatigue persisted 40 months after the infection, and prolonged symptoms and fatigue were present up to 18 months after the MERS infection.^{45,46} Interestingly, in our study, we have found that the strongest predictor of the persistent symptoms in recovered SARS-CoV-2 patients was the PTSD symptom severity. It is, therefore, possible that in a group of SARS-CoV-2 patients, protracted symptoms are closely related to PTSD symptomatology.⁴² A recent study revealed that psychosomatic complaints were increased during the pandemic, even in the general population.⁴⁷

CONCLUSION

Evidence accumulated to date suggests that mental health has been affected adversely in various ways during the ongoing SARS-CoV-2 pandemic. Patients affected by SARS-CoV-2 have higher rates of delirium, depression, anxiety, PTSD, and persistent symptoms such as fatigue. Cases of first-episode psychosis and mania in people with SARS-CoV-2 have also been reported. Future studies are needed to understand the long-term psychiatric morbidity of the SARS-CoV-2 pandemic and to identify in depth the possible risk and protective factors. In order to serve the needs of patients, the groups particularly vulnerable to the adverse psychiatric consequences of SARS-CoV-2 should be identified, and effective interventions should be implemented.

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