

# Clinical Features and Prognosis of Coronavirus Disease 2019-Related Psychosis: A Retrospective Case Series

## ABSTRACT

**Background:** It has been reported that coronavirus disease 2019 (COVID-19) may cause psychiatric disorders, but there are too many confounding factors in the various studies, making it difficult to draw accurate conclusions.

**Methods:** We analyzed the clinical features and treatment of patients with non-severe COVID-19 who were hospitalized in neurology and psychiatry departments due to acute psychiatric disorders and performed a descriptive analysis.

**Results:** Of the 57 patients included, 65% were hospitalized in the neurology department. Eighty-two percent of the patients exhibited abnormal mental behavior 1 week or less after COVID-19 diagnosis, and more than 60% of the patients had normal electroencephalogram (EEG), head imaging, autoimmune encephalitis antibody, and cerebrospinal fluid (CSF) results. Abnormal EEG results included an increase in nonspecific slow waves, abnormal imaging results included small ischemic areas and lacunar infarctions, and abnormal CSF results included a slight increase in cell numbers and protein levels and an increase in pressure. After administering antipsychotic drugs and/or immunotherapy, 67% of the patients experienced improvement in their psychiatric disorders by the time of discharge. Thirty-nine percent of the patients were discharged without antipsychotic medication and experienced no relapse of psychiatric symptoms.

**Conclusion:** Patients with non-severe COVID-19 and psychiatric disorders usually have a good prognosis and do not require long-term antipsychotic medication. Patients with uncontrollable mental symptoms experienced rapid remission after immunotherapy, suggesting that inflammation or the immune response may play an important role in the occurrence of simple acute psychiatric disorders caused by COVID-19.

Keywords: COVID-19, psychiatric disorders, antipsychotic medication, EEG, CSF

# Introduction

Human coronaviruses (HCoVs) during the pandemic have been associated with psychiatric disorders, and previous studies have reported psychiatric cases associated with severe acute respiratory syndrome (SARS), Middle East respiratory syndrome, and swine-origin influenza A (H1N1).<sup>1</sup> In the early stage of the coronavirus disease 2019 (COVID-19) pandemic, there were some reports of patients in Wuhan with COVID-19-related psychiatric disorders,<sup>2</sup> and subsequently, COVID-19-related mental disorders were reported in other countries.<sup>34</sup> Studies suggest that social factors (such as isolation-related stress),<sup>5</sup> viral infection of the central nervous system, indirect immune responses,<sup>6</sup> comorbidities, and therapeutic drugs (such as steroid withdrawal)<sup>7</sup> may be associated with neuropsychiatric diseases such as seizures, encephalopathy, stroke, delirium, demyelination, encephalomeningitis, acute necrotizing encephalitis, acute disseminated encephalomyelitis, and abnormal smell and taste.<sup>2,8-10</sup> However, the specific pathological mechanisms are still unclear.

The Chinese government lifted control measures for COVID-19 in December 2022, and since then, the clinical manifestations of most people infected with COVID-19 have been upper respiratory symptoms and pneumonia; however, there has also been an increase in



Copyright@Author(s) - Available online at alpha-psychiatry.com. Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License. Jinyuan Du<sup>1,\*</sup> Xiaobo Zhou<sup>2,\*</sup> Yi Guo<sup>1,3</sup> Fugui Jiang<sup>4,5</sup> Mengfan Yan<sup>6</sup> Qiong Zhu<sup>1,3</sup>

<sup>1</sup>Department of Neurology, Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, Chengdu, China

<sup>2</sup>Department of Psychosomatic, Sichuan Academy of Medical Sciences and Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, Chengdu, China

<sup>3</sup>Chinese Academy of Sciences Sichuan Translational Medicine Research Hospital, Chengdu, China

<sup>4</sup>Sichuan Provincial Center for Mental Health, Sichuan Academy of Medical Sciences and Sichuan Provincial People's Hospital, Chengdu, China

<sup>s</sup>Key Laboratory of Psychosomatic Medicine, Chinese Academy of Medical Sciences, Chengdu, China

<sup>6</sup>Chengdu University of Traditional Chinese Medicine, School of Public Health, Chengdu, China

\*Jinyuan Du and Xiaobo Zhou contributed equally to this work.

Corresponding author:

Qiong Zhu or Mengfan Yan Zhuqiong427@126.com or fan\_ ddou@163.com

Received: July 4, 2023 Accepted: November 22, 2023 Publication Date: December 29, 2023

Cite this article as: Du J, Zhou X, Guo Y, Jiang F, Yan M, Zhu Q. Clinical features and prognosis of coronavirus disease 2019-related psychosis: A retrospective case series. *Alpha Psychiatry*. 2023;24(6):276-282.

Alpha Psychiatry 2023;24(6):276-282

the number of patients hospitalized for acute psychiatric disorders in neurology and psychiatry departments. Moreover, most of these patients are asymptomatic or non-severe patients; they have no COVID-19 complications nor have they used hormones or other drugs. We propose that the appearance of these mental symptoms is directly related to viral infection. Herein, we analyzed and summarized the clinical features, drug use, and prognosis of patients with mild or asymptomatic COVID-19 who visited the neurology and psychiatry departments of our hospital due to psychiatric disorders after China lifted control measures for COVID-19. In addition to testing our hypotheses, we provide clinical data on the duration of antipsychotic drug use in these patients.

# **Material and Methods**

## **Data Sources and Approval**

Sichuan Provincial People's Hospital is a large-scale general hospital in Chengdu that has infectious disease and psychiatry departments. Since the outbreak of COVID-19, it has been a designated hospital for the treatment of individuals with COVID-19. Chengdu has a resident population of more than 20 million. We collected the data of patients who were hospitalized from December 2022 to February 2023 after COVID-19 control measures were lifted in the Department of Neurology and Department of Psychiatry of Sichuan Provincial People's Hospital due to mental and behavioral abnormalities. This study was approved by the Ethics Review Committee of Sichuan Provincial People's Hospital (Approval No: 伦审(研)2023年第148号, Date: April 12, 2023). This was a retrospective case series and thus did not adversely affect the rights and health of the subjects; therefore, individual consent was not needed. Our study complied with the general guidelines provided by the Strengthening the Reporting of Observational Studies in Epidemiology statement.<sup>11,12</sup>

## **Design and Data Extraction**

In April 2023, we screened discharged patients eligible for inclusion between December 10, 2022, and January 31, 2023, through the discharge diagnosis in the electronic medical records of the hospital's inpatient department. The information available in the electronic medical records includes general characteristics (age, sex, past history, severity of COVID-19, and time of mental symptoms following a COVID-19 diagnosis), laboratory and imaging data [cerebrospinal fluid, detection of auto-antibodies, electroencephalogram (EEG), magnetic resonance imaging (MRI), and computed tomography (CT)], length of hospitalization, treatment at hospital, etc.

Psychiatric symptom assessments and medical record reviews were jointly completed by 2 senior neurologists and 2 psychiatrists in the research team, and patients who met the inclusion criteria were as

# **MAIN POINTS**

- Coronavirus disease (COVID-19) can cause simple acute psychiatric disorders in patients with asymptomatic or non-severe COVID-19.
- Patients with COVID-19 who have psychiatric disorders usually have a good prognosis and do not require long-term antipsychotic medication.
- Appropriate immunotherapy is recommended for patients with COVID-19 who have uncontrollable mental symptoms or obvious abnormal electroencephalogram findings.

follows: (1) patients with mild or non-severe COVID-19 who tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (antigen or nucleic acid test) before or after admission; (2) patients who presented abnormal mental behavior on admission, with delusions, hallucinations, and confusion in speech, behavior, and thinking as the main clinical manifestations,<sup>12</sup> which could not be explained by underlying diseases other than COVID-19; (3) patients with the following discharge diagnosis: (i) organic psychiatric disorder or psychotic disorder or delirium associated with COVID-19 and viral encephalitis associated with COVID-19; (ii) COVID-19 classified<sup>13-15</sup> as (a) asymptomatic, i.e., no specific physical symptoms of COVID-19, (b) mild, i.e., nonspecific symptoms, such as fever, cough, sore throat, nasal congestion, physical discomfort, headache, muscle pain or physical discomfort, and no signs of pneumonia on imaging, or (c) mild pneumonia, i.e., symptoms of fever and respiratory tract infection, with pneumonia on imaging but no signs of severe pneumonia. For patients with uncertain diagnoses, the decision for inclusion was made by 4 doctors after a joint discussion. The exclusion criteria were as follows: (1) patients without COVID-19; (2) patients with psychotic symptoms related to other systemic diseases (such as hepatic encephalopathy, renal encephalopathy, pulmonary encephalopathy, and hyponatremia), encephalitis, dementia, poisoning, drug abuse, or steroid use; (3) patients with severe or critical pneumonia; and (4) patients who were missing much critical data (Figure 1).

On May 1, 2023, we conducted a telephone follow-up (mean follow-up of 3 months), which included psychiatric outcome (resolved at time of hospital discharge, resolved after discharge in 3 months, and not fully resolved within 3 months) and the withdrawal of antipsychotic medication (at discharge, discontinuation in 1 month, discontinuation in 3 months, and continuation after 3 months).



## Du et al. Clinical Features and Prognosis of COVID-19-Related Psychosis

## **Statistical Analysis**

The analysis employed descriptive statistical methods. Continuous variables with a normal distribution are presented as the mean (SD); nonnormal variables are reported as the median [interquartile range (IQR)]. Categorical variables descriptive statistics are given as frequencies with percentages. The data were analyzed by Statistical Package For The Social Sciences software, version 26.0 for Windows (IBM SPSS Corp.; Armonk, NY, USA).

# Results

## **Demographic Characteristics and Clinical Profile**

Table 1 shows the sociodemographic and clinical information of 57 patients [age median (IQR): 42 (28)], of whom 37 (65%) patients were hospitalized in the neurology department, 43 (75%) did not have any history of psychiatric disorders, 2 (4%) had a brief history of psychiatric disorders and a family history of psychiatric disorders, 6 (10%) patients had mental retardation, and 5 (9%) patients had only a family history of psychiatric disorders. Regarding COVID-19 severity, 14 (24%) patients were asymptomatic, 34 (60%) were diagnosed with mild COVID-19, and 9 (16%) were diagnosed with mild COVID-19 pneumonia. Forty-seven patients (82%) developed mental and behavioral abnormalities 1 week or less after infection, 9 (16%) patients developed mental and behavioral abnormalities 2 weeks after infection, and 1 (2%) patient developed mental and behavioral abnormalities within 1 month after infection.

While hospitalized, among the 50 (88%) patients who underwent lumbar puncture, 35 (70%) patients had normal cerebrospinal fluid (CSF), and 15 (30%) patients had abnormal CSF, i.e., slightly increased cell count (9 × 10<sup>6</sup>~16 × 10<sup>6</sup>/L), slightly increased protein concentration (0.46~0.88 g/L), and/or increased pressure (220~330 mmH<sub>2</sub>O). Thirty-eight patients were tested for autoimmune encephalitis antibodies using the cytometric beads array (CBA) method; 37 patients (73%) were negative and 1 (2%) patient was positive for anti-Ri antibody in serum. Regarding background EEG, 34 patients (60%) had

Table 1. General Characteristics of the 57 Patients	
Age (years)	
Median (IQR)	42 (28)
Men, n (%)	24 (42)
Source of patients	
Neurology	37 (65%)
Psychiatry/Psychosomatic medicine	20 (35%)
Psychiatric history	
None	43 (75%)
Acute transient mental disorder	2 (4%)
Mental retardation	6 (10%)
Family history of psychosis	6 (10%)
Severity of COVID-19	
Asymptomatic	14 (24%)
Mild COVID-19	34 (60%)
Mild pneumonia	9 (16%)
Time of mental symptoms after COVID-19 diagnosis	
One week or less	47 (82%)
Two weeks	9 (16%)
One month	1 (2%)
COVID 10 corona virus disease 2010: IOP interguartile range	

COVID-19, corona-virus disease 2019; IQR, interquartile range.

a normal EEG, 5 (9%) had an abnormal EEG, and 18 (32%) patients had no EEG. Among the patients with an abnormal EEG, 2 (4%) had increased frontal  $\theta$  waves, 2 (4%) had extensive  $\theta$  wave increases, and 1 (2%) patient had extensive  $\delta$  and  $\theta$  wave increases. Regarding head imaging, 45 patients (79%) had normal results, 7 (12%) had small ischemic foci and/or a small amount of demyelination in periventricular white matter on CT or MRI, and 1 (2%) patient had small ischemic foci and lacunar infarction on head MRI.

## **Treatment and Outcomes**

In terms of treatment, 28 (49%) patients were treated with antipsychotics and 2 (4%) of these patients were concurrently treated with modified electroconvulsive therapy (MECT). Dexamethasone or combination antipsychotic treatment was used in 14 (25%) patients, and 1 (2%) patient received MECT concurrently. Four patients (7%) received high-dose methylprednisolone or concurrent high-dose immunoglobulin/antipsychotic treatment. The remaining 11 (19%) patients received other treatments. Because most of the patients in this study had non-severe pneumonia and there was a shortage of antiviral drugs during the outbreak of COVID-19, only 2 (4%) patients used azvudine tablets, and 1 (2%) patient used Paxlovid. Benzodiazepines, ganciclovir, and piperacillin sodium/tazobactam sodium were also used by some patients. Among the 57 patients, 45 (79%) patients were discharged within 2 weeks, and 38 (67%) patients showed marked improvement or complete remission of psychiatric disorders at the time of discharge; the symptoms of 12 (21%) patients resolved within 3 months, including those of 4 (7%) patients with mental retardation. Five patients (9%) had not fully recovered 3 months after discharge, 4 (7%) reported anxiety and depressive symptoms, such as restlessness, impatience, depression, palpitation, and worry, and the other patient had residual mild delirium. One patient (2%) died (cause of death, unknown) and 1 patient (2%) was lost to follow-up. Antipsychotics were discontinued for 22 patients (39%) upon discharge, discontinued within 1 month after discharge for 10 patients (18%), and discontinued within 1 month to 3 months after discharge for 8 patients (14%); 15 patients (26%) continued to take medication 3 months after discharge, and the specific discontinuation time could not be determined for 1 patient (2%). Table 2 summarizes the results of the above analysis.

The recovery of patients with different treatment regimens was also assessed (Table 3 and Table 4). Among the 28 patients (49%) who were on antipsychotics, the mental symptoms of 14 (50%) had resolved by discharge. Mental symptoms had resolved in 9 patients (32%) by the follow-up at 3 months. The symptoms of 4 patients (14%) did not resolve, with 2 (7%) subsequently undergoing MECT. Of the 14 patients (25%) who received dexamethasone or combined antipsychotic treatment, 9 (64%) were in remission at discharge and 3 (21%) were in remission at the 3-month follow-up, including 1 (7%) who received MECT. Four patients treated with high doses of intravenous corticosteroids or concomitantly with gamma globulin (or in combination with antipsychotics) had fully recovered at discharge. Eleven patients (19%) on other treatment regimens had fully recovered at discharge.

# Discussion

In our study, most of the patients were women (n=33, 58%), and the average age of patients with COVID-19-related psychiatric disorders was 43 years, similar to the average age range of 40.3-43.9

Table 2. Summary of Laboratory and Imaging Data

, , , , ,	
CSF	
Normal	35 (61%)
Elevated intracranial pressure	8 (14%)
Pleocytosis	4 (7%)
Proteinorachia	9 (16%)
Unchecked	7 (12%)
Detection of auto-antibodies	
Negative	37 (73%)
Positive	1 (2%)
Unchecked	19 (33%)
EEG	
Normal	34 (60%)
Non-specific slowing with frontal area	2 (4%)
Diffuse theta activity	2 (4%)
Diffuse theta activity and delta activity	1 (2%)
Unchecked	18 (30%)
MRI or CT	
Normal	45 (79%)
Abnormal	8 (14%)
Unchecked	4 (7%)

Elevated CSF pressure was defined as >200 mmH<sub>2</sub>O. Pleocytosis is defined as  $\geq$ 5 cells/mm<sup>3</sup> and high proteinorachia as  $\geq$ 45mg/dL of CSF. We used immunoblot assay to detect neuronal intracellular antibodies and cell-based assay to detect neuronal surface antibodies in the serum and cerebrospinal fluid of the patients. CSF, cerebrospinal fluid; CT, computed tomography; EEG, electroencephalogram; MRI, magnetic resonance imaging.

Table 3. Clinical Interventions and Prognos	ses
Length of hospitalization	
One week or less	23 (40%)
Two weeks	22 (39%)
One month or more	12 (21%)
Therapy	
Only antipsychotics	28 (49%) (n = 2 with MECT)
Dexamethasone and/or antipsychotics	14 (25%) (n=1 with MECT)
High doses of gamma globulin and/or methylprednisolone or combinations with antipsychotics	4 (7%)
Other therapy	11 (19%)
Psychiatric outcomes	
Resolved by the time of hospital discharge	38 (67%)
Resolved within 3 months after discharge	12 (21%)
Not fully resolved within 3 months	5 (9%)
Passed away	1 (2%)
Unknown	1 (2%)
Withdrawal of antipsychotics	
At discharge	22 (39%)
Discontinuation in 1 month	10 (17%)
Discontinuation in 3 months	8 (14%)
Continuation after 3 months	16 (28%)
Unknown	1 (2%)
MECT, modified electroconvulsive therapy.	

years reported in studies conducted abroad.<sup>3,4,16</sup> The population of Chengdu is relatively concentrated, and the number of patients with acute psychiatric disorders suddenly increased after COVID-19 control measures were lifted. More than half of the patients (n = 37, 65%) in this study were hospitalized in neurology departments; in contrast, most foreign studies included patients at psychiatric hospitals or in hospital departments of psychiatry.<sup>34,16</sup> Our study used various sources of cases.

Seventy-six percent of patients had no prior history or family history of psychiatric disorders. This finding is consistent with multiple previous reports.<sup>16-18</sup> Our results further add to the existing data on the incidence of new psychosis in patients with COVID-19 and indicate that SARS-CoV-2 can cause acute psychotic episodes. The SARS-CoV-2 virus can easily invade the weak organs of patients.<sup>19,20</sup> Some patients with gastrointestinal dysfunction in the past have had mild respiratory symptoms but severe gastrointestinal symptoms after infection with SARS-CoV-2.<sup>21,22</sup> A total of 14 patients (24%) in our study had personal histories of psychiatric disorders and/or family histories of psychiatric disorders. They showed asymptomatic or mild symptoms after infection, but psychiatric disorders were prominent. Similar findings were also found in previous studies,<sup>16-18</sup> indicating that patients with previous mental and cognitive abnormalities have reduced brain function and are vulnerable to viral attacks.

The vast majority of COVID-19 patients (n=47, 82%) developed acute psychiatric symptoms within 1 week of infection, and a small number of patients (n=9, 16%) developed symptoms within 2 weeks. Similar results have been reported in foreign studies.<sup>23</sup> A very small number of patients (n = 1, 2%) developed psychiatric disorders within approximately 1 month of COVID-19 diagnosis. In neurology, this clinical picture needs to be differentiated from autoimmune encephalitis with abnormal mental behavior as the main manifestation. Patients with COVID-19-related encephalitis can also be positive for autoimmune antibodies, but the antibody positive rate is low.9 When COVID-19 causes psychiatric disorders in patients, most disorders are not accompanied by epileptic seizures.9 Only 1 patient (2%) in our study had epileptic seizures; in contrast, nearly 70% of patients with autoimmune encephalitis have epileptic seizures.<sup>24</sup> In our study, although COVID-19 caused the patients to present psychiatric symptoms, most of the patients had normal CSF, autoimmune antibodies, EEG, and brain MRI findings. Cerebrospinal fluid was abnormal in 26% of the patients, manifesting as mildly increased cell count and protein and increased intracranial pressure. One patient (2%) was positive for serum autoimmune encephalitis anti-Ri antibodies. The EEG and head MRI findings for anti-Ri antibody-positive patients were normal, and the psychiatric symptoms were difficult to control with paliperidone at first, with symptoms gradually resolving after intravenous corticosteroids and gamma globulin treatment. Ten percent of the patients showed a nonspecific slow-wave increase on EEG, and the abnormal psychiatric behavior of these patients had resolved by the time of hospital discharge, indicating that an abnormal EEG did not indicate a poor prognosis. Electrogram and head MRI findings for this patient were normal. Fourteen percent of patients showed small ischemic foci and/or a few paraventricular demyelinating lesions and small subcortical infarcts on CT or MRI. According to the imaging characteristics and the follow-up of the patient's condition, we believe that these imaging findings are not related to psychiatric disorders. However, a systematic review of case reports

Table 4. Psychiatric Outcomes with Different Therapies						
Psychiatric Outcomes	Only Antipsychotics, n = 28 (49%) (n = 2 with MECT)	Dexamethasone or/and Antipsychotics, n = 14 (25%) (n = 1 with MECT)	High Doses of Gamma Globulin and/or Methylprednisolone or Combinations with Antipsychotics, n = 4 (7%)	Other Therapy, n = 11 (19%)		
Resolved by the time of hospital discharge	14 (50%)	9 (64%)	4 (100%)	11 (100%)		
Resolved within 3 months of discharge	9 (32%)	3 (21%) (n = 1 with MECT)	-	-		
Not fully resolved within 3 months	4 (14%) (n = 2 with MECT)	1 (7%)	-	-		
Passed away	_	1 (7%)	_	-		
Unknown	1 (4%)	-	_	-		
MECT, modified electroconv	ulsive therapy					

of COVID-19-related encephalitis, meningoencephalitis, acute necrotizing encephalitis, and acute disseminated encephalomyelitis published before January 2021 by Raha Zamani et al<sup>9</sup> found that among 182 patients, approximately 50% had increased CSF cells and protein levels, with 78% and 93.2% having MRI and EEG abnormalities, respectively. This may be because the patients included in this study had few comorbidities or underlying diseases or because of infection with different SARS-CoV-2 strains.

There are no uniform diagnostic criteria for COVID-19-related psychiatric disorders or COVID-19-related encephalitis. We found that the discharge diagnoses for patients with COVID-19-related psychiatric disorders were mostly psychiatric disorders diagnosed in the department of psychiatry and mostly viral encephalitis diagnosed in the neurology department. Likewise, there is no uniform standard for treatment. Similar to many case reports.<sup>4,25-28</sup> the psychiatric symptoms of the majority of patients in our study were controlled after treatment with antipsychotics and/or low-dose corticosteroids. Fourteen patients (25%) received intravenous dexamethasone, and the psychiatric symptoms of 9 patients (64%) had resolved by discharge. For some patients, electroconvulsive therapy was effective.<sup>29,30</sup> Three patients (5%) in the psychiatric department were treated with electroconvulsive therapy. Although their psychiatric disorders resolved, they still had anxiety and depression during follow-up. These patients did not use intravenous corticosteroids or immunoglobulins. The patients who received intravenous corticosteroids and gamma immunoglobulin had severe abnormal EEG findings and difficult-to-control psychiatric symptoms and were anti-Ri antibody positive, and their mental behavior returned to normal at the time of discharge. Some studies have also found a significant improvement in COVID-19-related encephalitis and meningoencephalitis with intravenous corticosteroids or concomitant use with immunoglobulin.9 Therefore, it is still recommended to consider intravenous corticosteroids or concomitant use with immunoglobulins for patients who do not respond to antipsychotic drugs or psychotherapy in clinical practice or patients with obvious abnormal EEG or abnormal CSF findings or with autoimmune antibodies.

Overall, 38 (67%) patients had returned to normal at discharge, 22 (39%) discontinued antipsychotics at discharge, and 18 (31%) discontinued antipsychotics within 3 months of discharge. There was no abnormal mental behavior during follow-up for 3 months; therefore, the overall prognosis of psychiatric disorders caused by COVID-19 is good. Five patients (9%) had long-term COVID-19 symptoms,

such as anxiety and depression, which have been reported in other populations.<sup>32,33</sup> Through a case review, we found that these patients received different treatments but that the prognosis was good; therefore, it cannot be ruled out that the disease may be self-limiting in some patients. For the above reasons, we believe that most patients with psychiatric disorders caused by COVID-19 may need only short-term symptomatic treatment and can stop antipsychotics when they are no longer experiencing mental symptoms.

To rule out the complications of COVID-19 infection and psychiatric disorders caused by treatment drugs, the COVID-19 patients included in this study were asymptomatic and non-severe COVID-19 patients. Research results in other countries suggest that half of the COVID-19 patients with psychiatric disorders present with asymptomatic and mild COVID-19,<sup>3,4</sup> indicating that COVID-19 may lead directly to psychiatric disorders. Therefore, the study of psychiatric disorders caused by COVID-19 infection should serve as a reminder that in neurology and psychosomatic clinics, clinicians may encounter patients with acute psychiatric disorders who have had previous infections or suspected infections. After a series of examinations, the exact cause may not be found. If a clinician provides symptomatic treatment with antipsychotic drugs and the psychiatric symptoms resolve after a period of time, it cannot be ruled out that such patients may have been infected with a virus that triggered a neuroimmune response and resulted in a transient psychiatric disorder. Some patients have more severe psychiatric disorders, which may be related to a persistent immune response and require EEG, head MRI, and autoimmune antibody test to assist in diagnosis and treatment. The specific pathogenesis requires further in-depth research on neuroimmune responses.

This study focused on hospitalized patients with psychiatric disorders or delirium that manifested after acute infection; therefore, the study has some limitations. (1) The number of included patients was small. When COVID-19 was widespread in China, large numbers of medical staff also fell ill and found it difficult to devote themselves to their work during the acute disease phase. At that time, there were no investigations, research, or records of individuals in the community. During the COVID-19 pandemic, a large number of elderly patients were hospitalized due to lung infection. Medical resources were seriously insufficient. Some patients with psychiatric disorders could only go to the emergency department for treatment, and such patients were not included in our study. (2) Although this study involved 2 departments, it is still a single-center study. (3) The follow-up for this study was only 3 months; therefore, the long-term

#### Du et al. Clinical Features and Prognosis of COVID-19-Related Psychosis

prognosis of these patients is unknown. (4) Another limitation is that our study only assessed psychiatric disorders involving psychopathology and did not study patients with anxiety and depression.

In general, COVID-19 can cause acute psychotic symptoms or psychiatric symptoms in asymptomatic or non-severe patients, and most patients have no abnormal EEG, brain imaging, CSF, or autoimmune encephalitis antibody results. Appropriate immunotherapy is recommended for patients with obvious abnormal EEG findings or a poor response to antipsychotic drugs, but after symptomatic treatment with antipsychotic drugs, the psychiatric disorders resolved without recurrence after discharge for most patients, and they do not need to use antipsychotics long term. Fully understanding the clinical features of psychiatric disorders caused by COVID-19 will help neurologists and psychiatrists understand the etiology of acute psychiatric disorders and the duration of antipsychotic drug use. Furthermore, the follow-up of such patients may also improve clinicians' understanding of neuroimmune inflammatory responses.

Availability of Data and Materials: The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics Committee Approval: This study was approved by the Ethics Committee of Sichuan Provincial People's Hospital (Approval No: 伦审 (研) 2023年第148号, Date: April 12, 2023).

Informed Consent: Verbal informed consent was obtained from the patients who agreed to take part in the study.

#### Peer-review: Externally peer-reviewed.

Author Contributions: Concept – Q.Z., X.Z., Y.G., F.J.; Design – M.Y., Q.Z., X.Z., Y.G., F.J.; Supervision – Q.Z.; Resources – Q.Z.; Materials – X.Z., Y.G., F.J., Q.Z.; Data Collection and/or Processing – J.D., M.Y., Q.Z., X.Z., Y.G., F.J.; Analysis and/or Interpretation – M.Y., Q.Z., X.Z., Y.G., F.J.; Literature Search – J.D.; Writing – J.D., Q.Z.; Critical Review – X.Z., Y.G., F.J., M.Y., Q.Z.

Acknowledgments: We thank all the patients and their families for their participation in this study.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

## References

- Brown E, Gray R, Lo Monaco S, et al. The potential impact of COVID-19 on psychosis: A rapid review of contemporary epidemic and pandemic research. *Schizophr Res.* 2020;222:79-87. [CrossRef]
- Rogers JP, Chesney E, Oliver D, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. *Lancet Psychiatry*. 2020;7(7):611-627. [CrossRef]
- Iqbal Y, Al Abdulla MA, Albrahim S, Latoo J, Kumar R, Haddad PM. Psychiatric presentation of patients with acute SARS-CoV-2 infection: a retrospective review of 50 consecutive patients seen by a consultationliaison psychiatry team. *BJPsych Open*. 2020;6(5):e109. [CrossRef]
- Chaudhary AMD, Musavi NB, Saboor S, Javed S, Khan S, Naveed S. Psychosis during the COVID-19 pandemic: A systematic review of case reports and case series. J Psychiatr Res. 2022;153:37-55. [CrossRef]
- Brooks SK, Webster RK, Smith LE, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet*. 2020;395(10227):912-920. [CrossRef]

- Wu Y, Xu X, Chen Z, et al. Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain Behav Immun*. 2020;87:18-22. [CrossRef]
- D'Imperio A, Lo J, Bettini L, Prada P, Bondolfi G. Bipolar type I diagnosis after a manic episode secondary to SARS-CoV-2 infection: A case report. *Med (Baltim)*. 2022;101(31):e29633. [CrossRef]
- Varatharaj A, Thomas N, Ellul MA, et al. Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study. *Lancet Psychiatry*. 2020;7(10):875-882. (doi:[CrossRef]
- Zamani R, Pouremamali R, Rezaei N. Central neuroinflammation in Covid-19: a systematic review of 182 cases with encephalitis, acute disseminated encephalomyelitis, and necrotizing encephalopathies. *Rev Neurosci.* 2021;33(4):397-412. [CrossRef]
- Mastrangelo A, Bonato M, Cinque P. Smell and taste disorders in COVID-19: from pathogenesis to clinical features and outcomes. *Neurosci Lett.* 2021;748:135694. [CrossRef]
- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. 2007;370(9596):1453-1457. [CrossRef]
- 12. Owen MJ, Sawa A, Mortensen PB. Schizophrenia. *Lancet*. 2016;388(10039): 86-97. [CrossRef]
- 13. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. Bethesda (MD): National Institutes of Health. US; 2021.
- 14. Laine C, Cotton D, Moyer DV. Outpatient evaluation and management of COVID-19. Ann Intern Med. 2022;175(4):590-591. [CrossRef]
- 15. *Therapeutics and COVID-19: Living Guideline*. Geneva: World Health Organization; 2022.
- Smith CM, Gilbert EB, Riordan PA, et al. COVID-19-associated psychosis: A systematic review of case reports. *Gen Hosp Psychiatry*. 2021;73:84-100.
  [CrossRef]
- Taquet M, Geddes JR, Husain M, Luciano S, Harrison PJ. 6-month neurological and psychiatric outcomes in 236379 survivors of COVID-19: a retrospective cohort study using electronic health records. *Lancet Psychiatry*. 2021;8(5):416-427. [CrossRef]
- Parra A, Juanes A, Losada CP, et al. Psychotic symptoms in COVID-19 patients. A retrospective descriptive study. *Psychiatry Res.* 2020;291:113254. [CrossRef]
- Muralidar S, Ambi SV, Sekaran S, Krishnan UM. The emergence of COVID-19 as a global pandemic: understanding the epidemiology, immune response and potential therapeutic targets of SARS-CoV-2. *Biochimie*. 2020;179:85-100. [CrossRef]
- Raman R, Patel KJ, Ranjan K. COVID-19: unmasking emerging SARS-CoV-2 variants, vaccines and therapeutic strategies. *Biomolecules*. 2021;11(7):993. [CrossRef]
- 21. Ma C, Cong Y, Zhang H. COVID-19 and the digestive system. *Am J Gastroenterol.* 2020;115(7):1003-1006. [CrossRef]
- 22. Kariyawasam JC, Jayarajah U, Riza R, Abeysuriya V, Seneviratne SL. Gastrointestinal manifestations in COVID-19. *Trans R Soc Trop Med Hyg.* 2021;115(12):1362-1388. [CrossRef]
- Correa-Palacio AF, Hernandez-Huerta D, Gómez-Arnau J, Loeck C, Caballero I. Affective psychosis after COVID-19 infection in a previously healthy patient: a case report. *Psychiatry Res.* 2020;290:113115. [CrossRef]
- 24. Yeshokumar AK, Coughlin A, Fastman J, et al. Seizures in autoimmune encephalitis-A systematic review and quantitative synthesis. *Epilepsia*. 2021;62(2):397-407. [CrossRef]
- Tariku M, Hajure M. Available evidence and ongoing hypothesis on corona virus (COVID-19) and psychosis: is corona virus and psychosis related? A narrative review. *Psychol Res Behav Manag.* 2020;13:701-704. [CrossRef]
- Lorenzo-Villalba N, Jannot X, Syrovatkova A, Michel V, Andrès E. SARS-CoV-2 infection and psychiatric manifestations in a previous healthy patient. *Caspian J Intern Med.* 2020;11(suppl 1):566-568. [CrossRef]

#### Alpha Psychiatry 2023;24(6):276-282

#### Du et al. Clinical Features and Prognosis of COVID-19-Related Psychosis

- 27. Jaworowski S, Weiser M, Gropp C, Malka M. Three cases of COVID-19-related first onset brief reactive psychosis. *Isr Med Assoc J*. 2020;22(10):612.
- Haddad PM, Al Abdulla M, Latoo J, Iqbal Y. Brief psychotic disorder associated with quarantine and mild COVID-19. *BMJ Case Rep.* 2020; 13(12):e240088. [CrossRef]
- 29. Austgen G, Meyers MS, Gordon M, Livingston R. The use of electroconvulsive therapy in neuropsychiatric complications of coronavirus disease 2019: A systematic literature review and case report. *J Acad Consult Liaison Psychiatry*. 2022;63(1):86-93. [CrossRef]
- Chacko M, Job A, Caston F 3rd, George P, Yacoub A, Cáceda R. COVID-19-induced psychosis and suicidal behavior: case report. SN Compr Clin Med. 2020;2(11):2391-2395. [CrossRef]
- Raveendran AV, Jayadevan R, Sashidharan S. Long COVID: an overview [published correction appears in Diabetes Metab Syndr. 2022 May;16(5):102504] [published correction appears in Diabetes Metab Syndr. 2022 Dec;16(12):102660]. *Diabetes Metab Syndr.* 2021;16(12): 102660. [CrossRef]
- Aiyegbusi OL, Hughes SE, Turner G, et al. Symptoms, complications and management of long COVID: a review. *J R Soc Med.* 2021;114(9):428-442. [CrossRef]
- Davis HE, McCorkell L, Vogel JM, Topol EJ. Long COVID: major findings, mechanisms and recommendations. *Nat Rev Microbiol*. 2023;21(3):133-146. [CrossRef]