Underlying Mental Illness and Risk of Severe Outcomes Associated With COVID-19

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Background: According to the Centers for Disease Control and Prevention, depression and schizophrenia, among other conditions, put individuals at high risk for severe COVID-19 infection. Patients at high risk often are eligible for outpatient therapies, such as antiviral and monoclonal antibody therapies, to prevent severe infection. However, depression and schizophrenia are not considered risk factors for severe COVID-19 infection at the Captain James A. Lovell Federal Health Care Center in North Chicago, Illinois, making patients with these conditions ineligible for outpatient therapy unless they have another high-risk condition.
Methods: This retrospective cohort study assessed outcomes among patients with mild-to-moderate COVID-19 to determine whether depression and/or schizophrenia impacted the risk of

severe disease or negative outcomes. The primary outcome was severe COVID-19 outcomes defined as hospitalization, admission to the intensive care unit, intubation or mechanical ventilation, or death within 30 days of infection.
Results: Patients with depression or schizophrenia had more hospitalizations and deaths, but this difference was not statistically significant ($P = .36$). Death within 30 days of COVID-19 infection only occurred in patients with depression or schizophrenia.
Conclusions: Although there were more hospitalizations and deaths from COVID-19 within 30 days of infection among patients with depression and schizophrenia compared with individuals without these disorders, this finding was not statistically significant.

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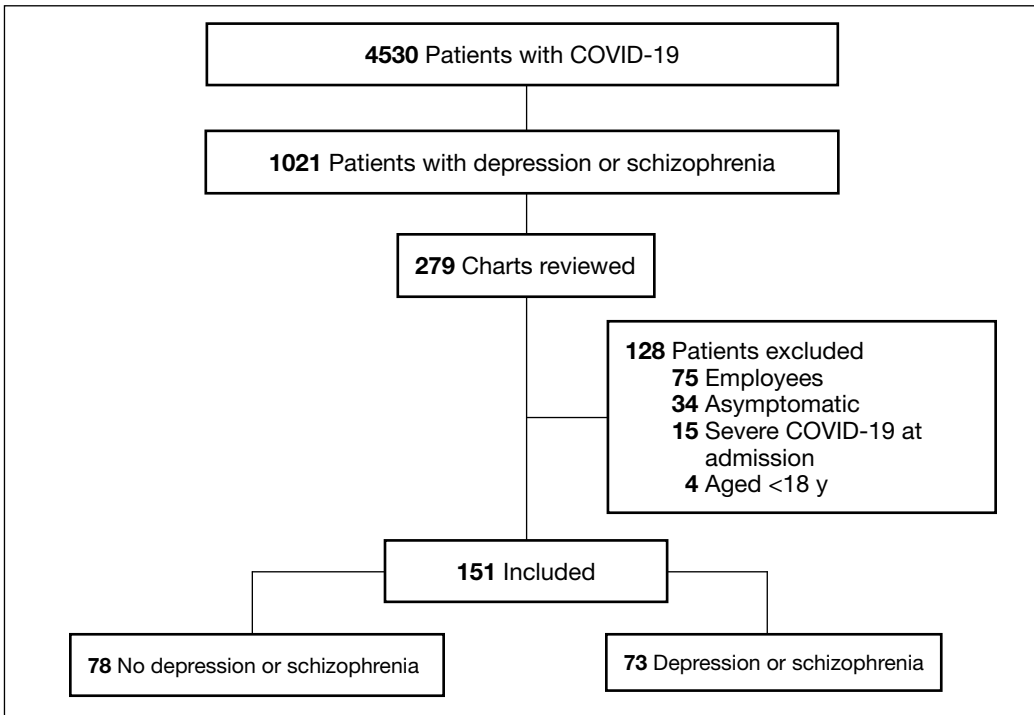Angelica Castro
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The Centers for Disease Control and Prevention (CDC) has identified factors that put patients at a higher risk of severe COVID-19 infection, which include advanced age, obesity, cardiovascular disease, diabetes, chronic kidney disease, lung disease, and immunocompromising conditions. The CDC also acknowledges that mood disorders, including depression and schizophrenia, contribute to the progression to severe COVID-19.[1] Antiviral therapies, such as nirmatrelvir and ritonavir combination, remdesivir, and molnupiravir, and monoclonal antibody (mAb) therapies, have been used to prevent hospitalization and mortality from COVID-19 infection for individuals with mild-to-moderate COVID-19 who are at high risk of progressing to severe infection.[2] Although antiviral and mAb therapies likely have mitigated many infections, poor prognoses are prevalent. It is important to identify all patients at risk of progressing to severe COVID-19 infection.

Although the CDC considers depression and schizophrenia to be risk factors for severe COVID-19 infection, the Captain James A. Lovell Federal Health Care Center (FHCC) in North Chicago, Illinois, does not, making these patients ineligible for antiviral or mAb therapies unless they have another risk factor. As a result, these patients could be at risk of severe COVID-19 infection, but might not be treated appropriately. Psychiatric diagnoses are common among veterans, with 19.7% experiencing a mental illness

in 2020.[3] It is imperative to determine whether depression or schizophrenia play a role in the progression of COVID-19 to expand access to individuals who are eligible for antiviral or mAb therapies.

Because COVID-19 is a novel virus, there are few studies of psychiatric disorders and COVID-19 prognosis. A 2020 case control study determined that those with a recent mental illness diagnosis were at higher risk of COVID-19 infection with worse outcomes compared with those without psychiatric diagnoses. This effect was most prevalent among individuals with depression and schizophrenia.[4] However, these individuals also were found to have additional comorbidities that could have contributed to poorer outcomes. A meta-analysis determined that psychiatric disorders were associated with increased COVID-19-related mortality.[5] A 2022 cohort study that included vaccinated US Department of Veterans Affairs (VA) patients determined that having a psychiatric diagnosis was associated with increased incidence of breakthrough infections.[6] Individuals with psychiatric conditions are thought to be at higher risk of severe COVID-19 outcomes because of poor access to care and higher incidence of untreated underlying health conditions.[7] Lifestyle factors also could play a role. Because there is minimal data on COVID-19 prognosis and mental illness, further research is warranted to determine

FIGURE Study Design Flowchart


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                    │   4530 Patients with COVID-19            │
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          ┌───────────────────────────────────────────────────┐
          │  1021 Patients with depression or schizophrenia    │
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                                      │
                        ┌──────────────────────────┐
                        │   279 Charts reviewed     │
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                                      │        │ 128 Patients excluded         │
                                      │        │   75 Employees                │
                                      │        │   34 Asymptomatic             │
                                      │        │   15 Severe COVID-19 at       │
                                      │        │       admission               │
                                      │        │    4 Aged <18 y               │
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                        │    151 Included           │
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┌─────────────────────────────────────┐   ┌─────────────────────────────────────┐
│ 78 No depression or schizophrenia    │   │ 73 Depression or schizophrenia       │
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whether psychiatric diagnoses could contribute to more severe COVID-19 infections.

METHODS

This was a retrospective cohort chart review study at FHCC that compared COVID-19 outcomes in individuals with depression or schizophrenia with those without these diagnoses. FHCC patients with the *International Classification of Diseases* code for COVID-19 (U07.1) from fiscal years 2020 to 2022 were included. We then selected patients with a depression or schizophrenia diagnosis noted in the electronic health record (EHR). These 2 patient lists were consolidated to identify every individual with a COVID-19 diagnosis and a diagnosis of depression or schizophrenia.

Patients were included if they were aged ≥ 18 years with a positive COVID-19 infection confirmed via polymerase chain reaction or blood test. Patients also had to have mild-to-moderate COVID-19 with ≥ 1 symptom such as fever, cough, sore throat, malaise, headache, muscle pain, loss of taste and smell, or shortness of breath. Patients were excluded if they had an asymptomatic infection, presented with severe COVID-19 infection, or were an FHCC employee. Severe COVID-19 was defined as

having oxygen saturation < 94%, a respiratory rate > 30 breaths per minute, or supplemental oxygen requirement.

Patient EHRs were reviewed and analyzed using the VA Computerized Patient Record System and Joint Legacy Viewer. Collected data included age, medical history, use of antiviral or mAb therapy, and admission or death within 30 days of a positive COVID-19 test. The primary outcome of this study was severe COVID-19 outcomes defined as hospitalization, admission to the intensive care unit, intubation or mechanical ventilation, or death within 30 days of infection. The primary outcome was analyzed with a student t test; $P < .05$ was considered statistically significant.

RESULTS

More than 5000 individuals had a COVID-19 diagnosis during the study period. Among these patients, 4530 had no depression or schizophrenia diagnosis; 1021 individuals had COVID-19 and a preexisting diagnosis of depression or schizophrenia. Among these 1021 patients, 279 charts were reviewed due to time constraints; 128 patients met exclusion criteria and 151 patients were included in the study. Of the 151 patients with COVID-19, 78 had no

TABLE 1 Baseline Risk Factors for Severe COVID-19

Risk factors	No depression/schizophrenia, No. (%) (n = 78)	Comorbid depression/schizophrenia, No. (%) (n = 73)
Age > 60 y	22 (28)	23 (32)
Diabetes	9 (12)	10 (14)
Cardiovascular disease	19 (24)	22 (30)
Lung disease	6 (8)	11 (15)
Obesity	20 (26)	21 (29)
Chronic kidney disease	3 (4)	1 (1)
Immunosuppressed	4 (5)	4 (5)
No comorbidities	44 (56)	30 (41)

Mood disorder
  Depression
  Schizophrenia
	–
	–
		67 (92)
		6 (8)

TABLE 2 COVID-19 Treatments

Regimens	No depression/schizophrenia, No. (%) (n = 78)	Comorbid depression/schizophrenia, No. (%) (n = 73)
Nirmatrelvir/ritonavir	8 (10)	8 (11)
Casirivimab/imdevimab	2 (3)	3 (4)
Bebtelovimab	0	2 (3)
Remdesivir	1 (1)	0
Total	11 (14)	13 (18)

depression or schizophrenia and 73 patients with COVID-19 had a preexisting depression or schizophrenia diagnosis (Figure).

The 2 groups were similar at baseline. The most common risk factors for severe COVID-19 included age > 60 years, obesity, and cardiovascular disease. However, more than half of the individuals analyzed had no risk factors (Table 1). Some patients with risk factors received antiviral or mAb therapy to prevent severe COVID-19 infection; combination nirmatrelvir and ritonavir was the most common agent (Table 2). Of the 73 individuals with a psychiatric diagnosis, 67 had depression (91.8%), and 6 had schizophrenia (8.2%).

Hospitalization or death within 30 days of COVID-19 infection between patients with depression or schizophrenia and patients without these psychiatric diagnoses was not statistically significant (P = .36). Sixteen individuals were hospitalized, 8 in each group. Three individuals died within 30 days; death only occurred in patients who had depression or schizophrenia (Table 3).

DISCUSSION

This study found that hospitalization or death within 30 days of COVID-19 infection occurred more frequently among individuals with depression or schizophrenia compared with those without these psychiatric comorbidities. However, this difference was not statistically significant.

This study had several limitations. It was a retrospective, chart review study, which relied on accurate documentation. In addition, we reviewed COVID-19 cases from fiscal years 2020 to 2022 and as a result, several viral variants were analyzed. This made it difficult to draw conclusions, especially because the omicron variant is thought to be less deadly, which may have skewed the data. Vaccinations and COVID-19 treatments became available in late 2020, which likely affected the progression to severe disease. Our study did

TABLE 3 Patient Outcomes

Outcomes within 30 d	No depression/schizophrenia, No. (%) (n = 78)	Comorbid depression/ schizophrenia, No. (%) (n = 73)	Total (N = 151)	*P* value
Hospitalization	8 (10)	8 (11)	16 (11)	.89
Death	0	3 (4)	3 (2)	.07
Total	8 (10)	11 (15)	19 (13)	.36

not assess vaccination status, therefore it is unclear whether COVID-19 vaccination played a role in mitigating infection. When the pandemic began, many individuals were afraid to come to the hospital and did not receive care until they progressed to severe COVID-19, which would have excluded them from the study. Many individuals had additional comorbidities that likely impacted their COVID-19 outcomes. It is not possible to conclude if the depression or schizophrenia diagnoses were responsible for hospitalization or death within 30 days of infection or if it was because of other known risk factors. Future research is needed to address these limitations.

CONCLUSIONS

More COVID-19 hospitalizations and deaths occurred within 30 days of infection among those with depression and schizophrenia compared with individuals without these comorbidities. However, this effect was not statistically significant. Many limitations could have contributed to this finding, which should be addressed in future studies. Because the sample size was small, further research with a larger patient population is warranted to explore the association between psychiatric comorbidities such as depression and schizophrenia and COVID-19 disease progression. Future studies also could include assessment of vaccination status and exclude individuals with other high-risk comorbidities for severe COVID-19 outcomes. These studies could determine if depression and schizophrenia are correlated with worse COVID-19 outcomes and ensure that all high-risk patients are identified and treated appropriately to prevent morbidity and mortality.

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Author Disclosures
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Ethics and consent
This project was approved by the Edward Hines, Jr. Veterans Affairs Hospital Institutional Review Board.

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