

History of Suicide Attempts and COVID-19 Infection in Veterans with Schizophrenia or Schizoaffective Disorder: Moderating Effects of Age and Body Mass Index

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Keywords

Veterans · Schizophrenia · Schizoaffective disorder · Suicide attempt · COVID-19

Abstract

Introduction: Relative to the general population, patients with schizophrenia or schizoaffective disorder have higher rates of suicide attempts and mortality from COVID-19 infection. Therefore, determining whether a history of suicide attempt is associated with COVID-19 in patients with schizophrenia or schizoaffective disorder has implications for COVID-19 vulnerability stratification in this patient population. **Methods:** We carried out cross-sectional analyses of electronic health records of veterans with a diagnosis of schizophrenia or schizoaffective disorder that received treatment at any United States Veterans Affairs Medical Center between January 1, 2020, and January 31, 2021. We used logis-

tic regression to estimate unadjusted and adjusted (including age, sex, race, marital status, body mass index (BMI), and a medical comorbidity score) odds ratios (ORs) for COVID-19 positivity in suicide attempters relative to nonattempters. **Results:** A total of 101,032 veterans (mean age 56.67 ± 13.13 years; males 91,715 [90.8%]) were included in the analyses. There were 2,703 (2.7%) suicide attempters and 719 (0.7%) patients were positive for COVID-19. The association between history of suicide attempt and COVID-19 positivity was modified by age and BMI, such that the relationship was only significant in patients younger than 59 years, and in obese (BMI ≥ 30) patients (adjusted OR 3.42, 95% CI 2.02–5.79 and OR 2.85, 95% CI 1.65–4.94, respectively). **Conclusions:** Higher rates of COVID-19 in young or obese suicide attempters with a diagnosis of schizophrenia or schizoaffective disorder might be due to the elevated risk for the infection in this subgroup of patients.

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Introduction

Schizophrenia is a severe mental illness affecting an estimated 20 million people worldwide [1], with a lifetime global prevalence of 0.4% [2]. However, the prevalence of schizophrenia ranged from 1.4% in a general veteran sample [3] and 11.2% in older adult veterans [4], compared to a range between 0.25% and 0.64% in nonveteran samples in the USA [3, 5, 6] suggesting a higher prevalence in the US veteran population. Of note, schizophrenia is associated with premature mortality particularly from suicide and comorbid somatic illnesses (especially complications of cardiovascular disease) [7, 8]. Furthermore, relative to the general population, patients with schizophrenia have a higher risk of contracting COVID-19 infection [9] (caused by the novel severe acute respiratory syndrome coronavirus 2[10]) which as of November 2021 has claimed over 5 million lives globally [11]. Patients with schizophrenia are also less likely to get vaccinated against COVID-19 [12]. Importantly, patients with schizophrenia who test positive for COVID-19 have a 2-fold increased risk of dying from the infection relative to individuals without mental illness [13]. There is therefore a need to identify vulnerability factors for COVID-19 in patients with schizophrenia which can guide the allocation of preventative and therapeutic resources and reduce mortality in this patient population.

Although factors associated with increased risk of contracting and dying from COVID-19 in the general population (e.g., unvaccinated status, older adult status, obesity, and pre-existing medical illnesses) [14–16] are likely to be relevant in patients with schizophrenia, other illness-specific factors might also elevate the risk of COVID-19 in patients. For example, patients with schizophrenia spectrum disorders who are treated with clozapine (an antipsychotic medication approved for treatment-resistant psychosis) have a higher risk of contracting COVID-19 than patients without a documented history of treatment with clozapine [17, 18]. Therefore, given that schizophrenia may be more prevalent among veterans [3, 4] and suicide attempts are relatively common in patients with schizophrenia (lifetime risk of 26.8% [19]) we sought to determine whether a history of suicide attempt in US veterans diagnosed with schizophrenia or schizoaffective disorder is positively associated with COVID-19 positivity. Since dimensions and behavioral traits (e.g., anhedonia, cognitive deficits, and impulsivity) associated with suicidal behavior [20] have also been associated with reduced propensity to adopt COVID-19 precautionary behaviors [21], we hypothesized that a history

of suicide attempt would be positively associated with COVID-19 positivity in veterans with schizophrenia or schizoaffective disorder.

Methods

Study Design, Setting, and Participant

We employed a cross-sectional design involving analyses of nationwide electronic health records (EHR) of a large sample of veterans with a diagnosis of schizophrenia or schizoaffective disorder that received treatment at any United States Veterans Affairs Medical Center (VAMC) between January 1, 2020, and January 31, 2021. The Institutional Review Board (IRB) of Baylor College of Medicine and the Michael E. DeBakey VAMC Research and Development Committee granted approval for this study (protocol # H-47313). The IRB granted a waiver of consent and HIPAA authorization since the use of deidentified protected health information involved no more than minimal risk (including privacy risks) to the individuals in this study.

Data Collection and Definitions

We collected data from the Corporate Data Warehouse (CDW) and the Veterans Affairs Informatics and Computing Interface (VINCI) [22]. The VA CDW incorporates data from EHR and several other sources throughout the Veteran's Health Administration into a single, standard database structure to facilitate reporting and data analysis. VINCI is a partner with the CDW and hosts all data available through CDW. However, if a veteran receives care at a non-VA healthcare facility, then the data for that encounter will not automatically be captured by CDW/VINCI.

The study team identified veterans with a diagnosis of schizophrenia or schizoaffective disorder and those with a documented history of suicide attempt by using the International Classification of Diseases, Ninth and Tenth Revisions codes (ICD-9 and ICD-10 codes). The ICD-9 and ICD-10 codes are provided in online supplementary Table 1 (for all online suppl. material, see www.karger.com/doi/10.1159/000521230). We also retrieved data on the outcome of interest, COVID-19-positive test results, from the EHR but we did not obtain data regarding the specific type of COVID-19 test. Veterans can request COVID-19 testing at no personal cost, but COVID-19 tests are not routinely ordered if a veteran is not admitted to an inpatient unit or undergoing diagnostic or therapeutic procedures such as electroconvulsive therapy (ECT). In addition, we extracted the following variables for each research subject: age (at last visit), sex, race, marital status, body mass index (BMI), and Charlson-Deyo score [23]. The Charlson-Deyo comorbidity index is a clinical comorbidity index which assigns a score to the various chronic medical conditions present in an individual patient and the sum of the scores is predictive of long-term mortality [24].

Statistical Analysis

We divided the sample of veterans with schizophrenia or schizoaffective disorder into 2 groups – suicide attempters and nonattempters. We then compared demographic and clinical variables between attempters and nonattempters using *t*-tests or χ^2 tests as appropriate. We have reported means and standard deviations for continuous variables and *n* (%) for categorical variables.

Table 1. Characteristics of the total sample of veterans with schizophrenia or schizoaffective disorder, suicide attempters, and nonattempters

Characteristics	Total sample (n = 101,032)	Attempters (n = 2,703)	Nonattempters (98,329)
Age (SD)	56.67±13.13	53.43±12.58	56.76±13.13
Sex, n (%)			
Male	91,715 (90.8)	2,349 (86.9)	89,366 (90.9)
Female	9,317 (9.2)	354 (13.1)	8,963 (9.1)
Race, n (%)			
White	55,941 (55.4)	1,765 (65.3)	54,176 (55.1)
Black	35,589 (35.2)	756 (28.0)	34,833 (35.4)
Asian	1,114 (1.1)	22 (0.8)	1,092 (1.1)
American-Indian or Alaska Native	1,003 (1.0)	34 (1.3)	969 (1.0)
Native Hawaiian or other Pacific Islander	1,155 (1.1)	23 (0.9)	1,132 (1.2)
Unknown	6,230 (6.2)	103 (3.8)	6,127 (6.2)
Marital status, n (%)			
Married	22,983 (22.7)	480 (17.8)	22,503 (22.9)
Divorced	29,656 (29.4)	1,029 (38.1)	28,627 (29.1)
Never married	38,671 (38.3)	918 (34.0)	37,753 (38.4)
Separated	5,604 (5.5)	165 (6.1)	5,439 (5.5)
Widowed	3,439 (3.4)	103 (3.8)	3,336 (3.4)
Single	223 (0.2)	6 (0.2)	217 (0.2)
Unknown	456 (0.5)	2 (0.1)	454 (0.5)
BMI category, n (%)			
Obese	40,717 (40.3)	1,069 (39.5)	39,648 (40.3)
Not obese	60,315 (59.7)	1,634 (60.5)	58,681 (59.7)
Total Deyo score (SD)	0.68±1.42	0.82±1.57	0.67±1.41

Total Deyo score is an indicator of long-term mortality and higher scores indicate higher medical comorbidities.

We applied logistic regression models to estimate the odds of testing positive for COVID-19 and comparing attempters to nonattempters, with additional analysis adjusting for age, sex, race, marital status, BMI, and total Charlson-Deyo score. Based on previous findings of higher vulnerability to a more severe COVID-19 illness in older adults [14], obese [15], and those with comorbid medical conditions [16], we also fitted COVID-19 status-by-age, COVID-19 status-by-BMI, and COVID-19 status by Charlson-Deyo score interactions in logistic regression models. We carried out stratified analyses for significant interactions. Stratified analyses were performed in patients younger than 59 years (the median age of the sample), patients older than 59 years, obese (BMI ≥ 30), and nonobese patients (BMI < 30), respectively. *p* values less than 0.05 were considered statistically significant. All statistical analyses were performed with IBM SPSS, Version 27 (IBM Corp., Armonk, NY, USA).

Results

A total of 101,032 veterans (mean age 56.67 \pm 13.13 years; males 91,715 [90.8%]) with either schizophrenia or schizoaffective disorder were included in the analyses. Of

these, 2,703 (2.7%) patients had a history of suicide attempt. Table 1 shows the demographic and clinical characteristics of suicide attempters and nonattempters. The mean age of suicide attempters was 53.4 \pm 12.6 years and the mean age of nonattempters was 56.8 \pm 13.1. Suicide attempters were more likely to be female (13.1% of attempters vs. 9.1% of nonattempters). There were a total of 719 (0.7%) COVID-positive cases in the entire sample. Table 2 shows the demographic and clinical characteristics of the COVID-positive and not COVID-positive groups, respectively.

History of Suicide Attempt and COVID-19 Positivity in the Entire Sample

There was a higher percentage of COVID-positive cases in attempters relative to nonattempters (Table 3), but this was not statistically significant (1.0% vs. 0.7%, $\chi^2 = 3.24$, *p* = 0.072). The unadjusted odds ratio (OR) for COVID positivity in patients with a history of suicide attempt was 1.42 (95% CI 0.97–2.10) and the adjusted OR was 1.90 (95% CI 1.28–2.80).

Table 2. Characteristics of COVID-19-positive and not COVID-19-positive veterans with schizophrenia or schizoaffective disorder

Characteristics	COVID-19-positive (n = 719)	Not COVID-19-positive (100,313)
Age (SD)	66.18±12.46	56.60±13.11
Sex, n (%)		
Male	681 (94.7)	91,034 (90.7)
Female	38 (5.3)	9,279 (9.3)
Race, n (%)		
White	378 (52.6)	55,563 (55.4)
Black	285 (39.6)	35,304 (35.2)
Asian	2 (0.3)	1,112 (1.1)
American-Indian or Alaska Native	8 (1.1)	995 (1.0)
Native Hawaiian or other Pacific Islander	9 (1.3)	1,146 (1.1)
Unknown	37 (5.1)	6,193 (6.2)
Marital status, n (%)		
Married	134 (18.6)	22,849 (22.8)
Divorced	210 (29.2)	29,446 (29.4)
Never married	288 (40.1)	38,383 (38.3)
Separated	42 (5.8)	5,562 (5.5)
Widowed	34 (4.7)	3,405 (3.4)
Single	5 (0.7)	218 (0.2)
Unknown	6 (0.8)	450 (0.4)
BMI category, n (%)		
Obese	250 (34.8)	40,467 (40.3)
Not obese	469 (65.2)	59,846 (59.7)
Total Deyo Score (SD)	1.34±2.01	0.67±1.40

Total Deyo score is an indicator of long-term mortality and higher scores indicate higher medical comorbidities.

Table 3. Number and percentage of COVID-19-positive cases based on suicide attempter/nonattempter status in the total sample and the subgroups of veterans with schizophrenia or schizoaffective disorder

Group	COVID-19-positive cases, n (%) in attempters	COVID-19-positive cases, n (%) in nonattempters	p value*
Total sample (n = 101,032)	27 (1.0)	692 (0.7)	0.072
Younger than 59 years (n = 50,490)	16 (1.0)	137 (0.3)	<0.001
Older than 59 years (n = 50,542)	11 (1.0)	555 (1.1)	0.884
Obese (40,717)	14 (1.3)	236 (0.6)	0.008
Not obese (60,315)	13 (0.8)	456 (0.8)	0.886

* Fisher's exact test.

Results of Subgroup Analyses

COVID-19 status-by-age and COVID-19 status-by-BMI interactions were significant ($B = -0.018$, $p < 0.001$ and $B = 0.772$, $p = 0.05$, respectively), but COVID-19 status by Charlson-Deyo score was not significant ($B = -0.042$, $p = 0.612$). In patients younger than 59 years, and in the obese patients, respectively, history of suicide attempt was associated with COVID-positive status in un-

adjusted analyses (OR 3.53 [95% CI 2.10–5.94]; OR 2.22 [95% CI 1.29–3.81]) and adjusted analyses (OR 3.42 [95% CI 2.02–5.79]; OR 2.85 [95% CI 1.65–4.94]). In patients older than 59 years, and in the nonobese patients, there was no statistically significant association between history of suicide attempt and COVID-19 positivity from the unadjusted and adjusted analyses (Table 4).

Table 4. Odds ratios (ORs) for COVID-19 positivity based on suicide attempt status (attempters vs. nonattempters) in the total sample and subgroup of veterans with schizophrenia or schizoaffective disorder

Group	Unadjusted OR with 95% CI	Adjusted OR with 95% CI*
Total sample (<i>n</i> = 101,032)	1.42 (0.97–2.10)	1.90 (1.28–2.80)
Younger than 59 years (<i>n</i> = 50,490)	3.53 (2.10–5.94)	3.42 (2.02–5.79)
Older than 59 years (<i>n</i> = 50,542)	0.91 (0.50–1.66)	0.91 (0.50–1.66)
Obese (<i>n</i> = 40,717)	2.22 (1.29–3.81)	2.85 (1.65–4.94)
Not obese (<i>n</i> = 60,315)	1.02 (0.59–1.78)	1.39 (0.80–2.43)

* Adjusted for age, sex, race, marital status, BMI, and total Charlson-Deyo score.

Discussion

In this nationwide Veterans Health Administration study, a history of suicide attempt was associated with testing positive for COVID-19 in veterans with schizophrenia or schizoaffective disorder who were either younger than 59 years or obese. In the entire sample, the unadjusted OR for the association of history of suicide attempt with COVID-19 positivity was not statistically significant but the adjusted OR was significant, a finding likely due to negative confounding (i.e., significant association of a covariate with the outcome) [25]. To our knowledge, this is the first study to report an association between history of suicide attempt and COVID-19 in veterans with schizophrenia or schizoaffective disorder.

The association of history of suicide attempt with COVID-19 in veterans with schizophrenia or schizoaffective disorder may be explained by psychological factors which both predispose patients to suicide attempts and make them more vulnerable to COVID-19 infection. For example, anhedonia, impulsivity, and substance use are associated with suicidal behavior and have also been associated with less likelihood of adopting COVID-19 precautionary behaviors such as physical distancing, wearing mask, or handwashing [21, 26]. Reverse causality is also possible; in other words, veterans with COVID-19 infection may have a higher risk of suicidal behavior [27]. However, given that COVID-19 has been in existence for approximately 2 years and we did not limit suicide attempts to those that only occurred since the beginning of the pandemic, our data do not support reverse causality.

The association of history of suicide attempt with COVID-19 positivity in the younger and obese subgroups is also noteworthy considering previous research findings. For example, suicide risk in schizophrenia is highest for young adults but lowest for patients older than 65 years

[8] and although BMI has not been associated with suicide risk in schizophrenia or schizoaffective disorder, obesity is associated with higher levels of immune system dysregulation and inflammation in patients with schizophrenia [28, 29]. Relatedly, markers of immune dysregulation and inflammation in the periphery and central nervous system are elevated in suicide attempters relative to nonattempters [30, 31]. Furthermore, primary humoral immunodeficiencies were recently robustly associated with psychiatric disorders (including schizophrenia) and suicide attempts in the same cohort [32]. It is, therefore conceivable, although speculative, that the association of suicide attempt history with COVID-19 might reflect dysregulated immune function in young and obese attempters, respectively, since individuals with conditions involving immune system dysregulation such as asthma and allergic rhinitis, are more likely to test positive for COVID-19 [33] relative to those without such conditions.

Due to possible long-term neuropsychiatric sequelae of COVID-19 infection [34], patients with schizophrenia or schizoaffective disorder who have a history of suicide attempt and are younger than 59 or obese, should be monitored closely since they may be more at risk of COVID-19. Indeed, there is the possibility of symptom exacerbation in patients with a history of suicide attempt who test positive for COVID-19 since postmortem examination of brains of individuals diagnosed with severe COVID-19 infection revealed COVID-19-related impaired brain neurotransmission [35]. COVID-19 prevention should therefore be emphasized and incorporated into the routine care of patients with schizophrenia or schizoaffective disorder who have a history of suicide attempt. For example, mental health providers should routinely educate patients on COVID-19 precautions such as wearing a mask, physical distancing, washing hands, and getting vaccinated. Patients should also be educated on com-

mon COVID-19 symptoms and the need to seek medical attention if they experience such symptoms.

This study is subject to several limitations. First, the cross-sectional design makes it impossible to infer a causal association between suicide attempt and COVID-19. Second, we do not have data on the specific nature and severity of suicide attempts. Third, the sample was predominantly male which limits the generalizability of our results. Fourth, we were unable to adjust for psychotropic medications, especially clozapine which has been associated with increased likelihood of testing positive for COVID-19 [18]. Finally, we did not have information on illness severity and so did not adjust for it. Related to the last limitation is our inability to control for ECT and inpatient versus outpatient status since patients treated with ECT and inpatients are more likely to get tested for COVID-19.

In summary, our findings provide preliminary evidence of an association between history of suicide attempt and COVID-19 in a subgroup of patients with schizophrenia or schizoaffective disorder and therefore support the expansion of strategies to ensure vaccination of patients with schizophrenia or schizoaffective disorder, especially given the fact that patients with schizophrenia are under-vaccinated against COVID-19 [12]. Future well-powered, prospective studies are needed to confirm our observed association between history of suicidal behavior and COVID-19 in patients with schizophrenia or schizoaffective disorder and also to elucidate the underlying mechanisms of the association.

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Statement of Ethics

This study was approved by the Institutional Review Board (IRB) of Baylor College of Medicine and the Michael E. DeBakey VAMC Research and Development Committee (protocol No. H-47313). The IRB granted a waiver of consent and HIPAA authorization since the use of deidentified protected health information involved no more than minimal risk (including privacy risks) to the individuals in this study.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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This was an unfunded study.

Author Contributions

O.O.O. conceived the original idea; A.W. and B.G.M. obtained the data; O.O.O. and A.W. analyzed the data; R.L.K., G.M.P., R.E.P., and T.B.B. made critical contributions to the interpretation of the results; and O.O.O. took the lead in writing the manuscript with contribution from all authors. All authors read and approved the final manuscript.

Data Availability Statement

The data that support the findings of this study are not publicly available, but a minimal data set required to replicate the study findings reported in the article will be made available on request to the corresponding author.

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