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Review

Do patients with schizophrenia have higher infection and mortality rates due to COVID-19? A systematic review

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ABSTRACT

People with mental illness are known to have poorer physical health outcomes. Among them, patients with schizophrenia spectrum disorders are disproportionately burdened. A number of recent studies have highlighted that patients with schizophrenia are particularly at risk from COVID-19. The aim of this systematic review was to clarify whether patients with schizophrenia spectrum disorders are at greater risk for poor COVID-19 outcomes. We conducted a systematic review of the literature following the PRISMA guidelines, using PubMed, PsycINFO (via Ovid) and Scopus as databases, to identify all studies which investigated infection and/or mortality rate from SARS-CoV-2 in patients with schizophrenia spectrum disorders. Following a formal screening process, seven studies met our inclusion criteria. The results of these seven studies were reported using odds ratios or adjusted odds ratios. The collective results indicated a moderate, but statistically significant effect for higher infection rates, and a strong statistically significant effect for higher mortality rates in patients with schizophrenia. Our findings indicate that people with schizophrenia have a high risk of being infected by the new coronavirus and have a significantly higher mortality rate than the general population. There are contradictory findings concerning other outcomes, including the frequency of intensive care unit admissions for this group. Collectively, these results indicate that people with schizophrenia spectrum disorders may be more vulnerable to being infected and more likely to die due to COVID-19, and yet their access to Intensive Care Units does not seem to be higher. We conclude that patients with schizophrenia constitute a vulnerable group for COVID-19 related infection and mortality, consequently there is a necessity for this vulnerable group of people to have better access to healthcare, including priority in nationwide COVID-19 vaccination programs and expedited intensive care treatment. Our conclusion adds to the ongoing debate arguing for equitable access to healthcare for people with schizophrenia spectrum disorders.

KEYWORDS: Schizophrenia, COVID-19, mortality, infection, equity, access to care, vaccination.

Introduction

The relationship between COVID-19 and mental disorders is bidirectional, because mental disorders may be a risk factor for COVID-19, and conversely COVID-19 patients present frequently with psychiatric problems.[1] In addition, the stress resulting from isolation and social alienation during lockdown periods may result in psychological problems.[2]

The COVID-19 pandemic is a great threat to health care systems across the world. The disease mostly affects vulnerable groups with established risk factors, such as older age, male sex, cardiovascular diseases, diabetes and neoplasms. Many of these factors are found in mental health patients and especially those suffering from schizophrenia.[3,4]

It is reported that mechanical ventilation, admission to an intensive care unit and death are more likely adverse outcomes among COVID-19 patients who are also diagnosed with mental disorders.[5]

Therefore, it would be very interesting to elucidate whether (a) patients with schizophrenia are more frequently infected with SARS-CoV-2, and (b) schizophre-

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nia is associated with higher mortality from COVID-19. This is a systematic review which tries to answer these two questions.

Methods

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[6]

Search strategy and inclusion criteria of studies

To identify relevant research papers, the two authors independently searched MEDLINE, Scopus and PsycINFO (via Ovid) up to 21/3/2021 using the key terms "Schizophrenia" AND "COVID-19". The resulting papers were then screened to include all those examining COVID-19 related infection or mortality, and to exclude thematically irrelevant studies (i.e., those not dealing with the aforementioned themes). Other inclusion/exclusion criteria were English language and adult population. Final paper inclusion was decided by consensus. External arbitration was planned for potential disagreements. References of included articles were also searched for citations of further relevant published and unpublished studies.

Data synthesis and outcome measures

Data extraction included article ID, time of publication, number of subjects, infection rate and/or mortality rate. The outcome measures were (a) SARS-CoV-2 infection rate in patients with schizophrenia, and (b) death of patients with schizophrenia from SARS-CoV-2. Both outcome rates (infection and mortality) were reported as Odds Ratios (OR)/Adjusted Odds Ratios (AOR).

Results

Study characteristics

Our searches in the three databases yielded 605 hits, which were reduced after duplicate and title/abstract screening to 16. Of the remaining 16 articles, 8 were excluded because they did not focus on the infection and/or mortality rate of patients with schizophrenia and COVID-19. Subsequently, one article was excluded at the full-text stage due to irrelevance. Therefore, 7 studies were included in the systematic review. The remaining 7 papers included 90,076 positive patients for SARS-CoV-2, among which 1,989 suffered from schizophrenia.

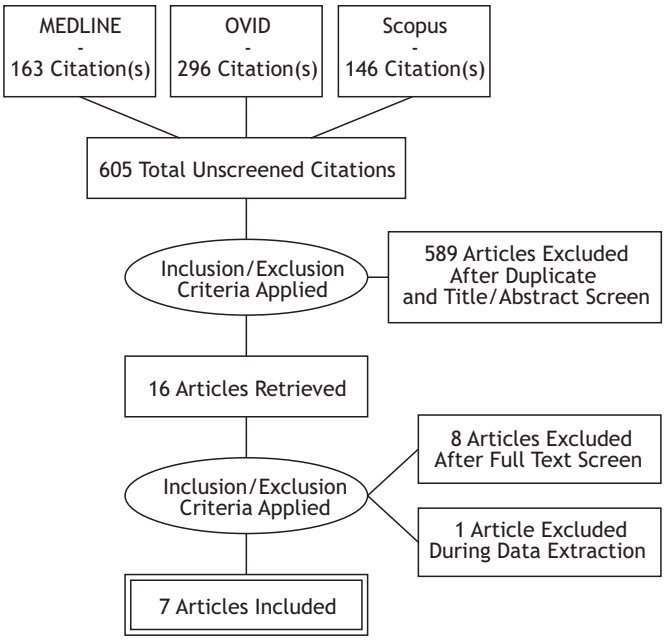

Figure 1. PRISMA flow diagram.

Infection and mortality rate

A large study from the USA[7] asserts that patients with schizophrenia have a higher infection rate compared to the rest of the population. The authors examined 15,110 patients with COVID-19 and found that patients with a recent diagnosis of schizophrenia had higher odds of contracting SARS-CoV-2 than the rest of the population (AOR=1.53, 95% CI:1.21-1.94, p<0.0001).

Two similar studies were conducted in Korea,[8,9] which studied 14,418 SARS-CoV-2 positive people. Patients with schizophrenia-related disorders had a higher risk of infection in both studies (OR=1.50, 95%CI:1.14–1.99, OR, 1.614–1.721). Moreover, schizophrenia patients experienced more severe outcomes of the infection, including death (OR=2.25, 95%CI:0.36–14.03), intensive care unit (ICU) admission, use of mechanical ventilation and acute respiratory distress syndrome (OR=1.27, 95%CI:0.37–4.37).

In Europe, there are two French studies[10,11] with 51,842 COVID-19 positive patients. These studies showed that schizophrenia is associated with increased in-hospital mortality (AOR=4.36, 95%CI:1.09–17.44, p=0.038 and OR 1.30 [95% CI, 1.08–1.56]) but not with increased intensive care unit admission. Schizophrenia patients between 65 and 80 years had a significantly higher risk of death than controls of the same age (+7.89%). Schizophrenia patients younger than 55 years had more ICU admissions (+13.93%) and Schizophrenia patients between 65 and 80 years and older than 80

years had fewer ICU admissions than controls of the same age (−15.44% and −5.93%, respectively).

Conversely, a study from Israel found that individuals with schizophrenia were less likely to test positive for COVID-19; however, they were twice as likely to be hospitalized for COVID-19 (OR 1.88 95% CI 1.39–2.55, P<0.0001). Furthermore, they were 3 times more likely to die from COVID-19 (OR 3.27 95% CI 1.39–7.68, P<0.0001), compared to the rest of the population.[12]

Another important finding in the literature was that patients with schizophrenia have a higher mortality rate for up to 45 days after a laboratory-confirmed positive SARS-CoV-2 test result.[13] In this study, 7348 COVID-19 positive patients, among them 75 with schizophrenia spectrum disorders (SSD), were followed up for 45 days. A premorbid diagnosis of schizophrenia spectrum disorders was significantly associated with mortality (OR=2.67; 95% CI, 1.48-4.80).

A summary of the results of these studies is shown in table 1.

Discussion

Our review shows that patients with schizophrenia have higher infection and mortality rates from SARS-CoV-2 compared to the rest of the population. This finding may be due to many factors.[14]

Firstly, many patients with schizophrenia suffer physical comorbidities, such as the metabolic syndrome. Mortality from COVID-19 is particularly elevated in people with comorbid conditions, in particular cardiovascular disease, diabetes, and chronic respiratory disease, all of which are more common in people with schizophrenia than the general population.[15–17] Moreover, patients with schizophrenia tend not to adhere well to their treatment, including treatment for physical illness. Consequently, their physical health is often poor. Similarly, it may be harder for people with schizophrenia to adopt and adhere to measures against infection (e.g., hand washing, social distancing or isolation, confinement), thus predisposing them to infection. The combination of poor physical health and a higher infection risk can prove fatal.

Smoking is another important factor for poor outcomes from COVID-19 in people with schizophrenia. Smoking is very prevalent in schizophrenia, with more than 60% of patients smoking. Smoking may worsen prognosis in COVID-19,[18] possibly because of its effect on the respiratory system and immune responsiveness.[19] In addition, many chronic patients with schizophrenia reside in long-term psychiatric facilities, so there is a high chance of conducting the virus to other patients if the environment is crowded.[11]

Furthermore, vulnerability to infection from Sars-Cov-2 may increase by the presence of pro-inflammatory factors postulated to occur in patients with schizophrenia.[20]

Finally, stigma puts people with schizophrenia at great risk for COVID-19. They face difficulties in accessing healthcare and often experience discrimination when they do access care. They are less likely to have a prompt and appropriate diagnostic work-up and therefore they are likely to have physical problems underdiagnosed or misdiagnosed, resulting in poor quality of care overall.[21,22]

Conclusion

In conclusion, people with schizophrenia spectrum disorders constitute a vulnerable group to COVID-19. Specifically, they suffer higher rates of infection and are more likely to die from COVID-19. Mitigating measures should be taken to ensure that people with schizophrenia are protected. We concur with Suhas23 that people

Table 1. Studies with patients with schizophrenia spectrum disorders (SSD) and COVID-19: Infection and mortality rates.

Study	Year	Patients with COVID-19	Infection rate of patients with SSD with COVID-19 (OR/AOR, [95% C.I.])	Mortality rate of patients with SSD from COVID-19 (OR/AOR, [95% C.I.])
Wang et al[7]	2021	15,110	1.53 [1.21-1.94]	
Jeon et al[8]	2021	7,077	1.50 [1.14-1.99]	2.25 [0.36-14.03]
Fond et al[10]	2020	1,092		4.36 [1.09-17.44]
Fond et al[11]	2020	50,750	1.30 [1.08–1.56]	
Nemani et al[13]	2020	7,348		2.67 [1.48-4.80]
Ji et al[9]	2020	7,341	? [1.614–1.721]	
Tzur Bitan et al[12]	2021	1,358		3.27 [1.39–7.68]

Note: OR, Odds Ratio; AOR, Adjusted Odds Ratio

with schizophrenia should be given priority to vaccination. We support that emphasis should be given to infection control measures, early recognition of COVID-19 symptoms, better access to healthcare and in particular intensive care, and stigma reduction. We conclude that the COVID-19 pandemic has disproportionately affected people with schizophrenia, making measures to ensure equitable care not just an option, but a necessity.

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Ανασκόπηση

Έχουν οι ασθενείς με σχιζοφρένεια υψηλότερη συχνότητα λοίμωξης και θνησιμότητας από τον COVID-19; Συστηματική ανασκόπηση

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ΠΕΡΙΛΗΨΗ

Είναι γνωστό πως ασθενείς με ψυχικές νόσους έχουν επιβαρυμένη σωματική υγεία σε σχέση με τον γενικό πληθυσμό. Μεταξύ των ασθενών με ψυχικές νόσους, εκείνοι με διαταραχές του φάσματος της σχιζοφρένειας έχουν δυσανάλογα μεγαλύτερη επιβάρυνση. Πρόσφατες μελέτες έχουν επισημάνει ότι αυτοί οι ασθενείς διατρέχουν ιδιαίτερο κίνδυνο από τον COVID-19. Στόχος αυτής της συστηματικής ανασκόπησης είναι να διευκρινιστεί κατά πόσον οι ασθενείς με διαταραχές του φάσματος της σχιζοφρένειας διατρέχουν μεγαλύτερο κίνδυνο για δυσμενείς εκβάσεις της σωματικής τους υγείας λόγω του COVID-19. Πραγματοποιήσαμε αυτή τη συστηματική ανασκόπηση της βιβλιογραφίας σύμφωνα με τις κατευθυντήριες γραμμές PRISMA, χρησιμοποιώντας το PubMed, το PsycINFO και το Scopus ως βιβλιογραφικές βάσεις δεδομένων, για να εντοπίσουμε όλες τις μελέτες που διερεύνησαν τη συχνότητα λοίμωξης ή/και θνησιμότητας από τον SARS-CoV-2 σε ασθενείς με διαταραχές του φάσματος της σχιζοφρένειας. Μετά από συστηματική διαδικασία ελέγχου, επτά μελέτες πληρούσαν τα κριτήρια ένταξής στη μελέτη. Τα αποτελέσματα αυτών των επτά μελετών εκτέθηκαν περιληπτικά χρησιμοποιώντας odds ratios ή adjusted odds ratios. Τα συλλογικά αποτελέσματα έδειξαν μέτρια, αλλά στατιστικά σημαντική επίδραση για υψηλότερα ποσοστά λοίμωξης σε ασθενείς με σχιζοφρένεια και ισχυρή στατιστικά σημαντική επίδραση για υψηλότερα ποσοστά θνησιμότητας σε ασθενείς με σχιζοφρένεια. Τα ευρήματά μας δείχνουν ότι τα άτομα με σχιζοφρένεια έχουν υψηλό κίνδυνο να μολυνθούν από τον νέο κορωνοϊό και έχουν σημαντικά υψηλότερο ποσοστό θνησιμότητας από τον γενικό πληθυσμό. Υπάρχουν αντιφατικά ευρήματα σχετικά με άλλα αποτελέσματα, συμπεριλαμβανομένης της συχνότητας εισαγωγής σε μονάδες εντατικής θεραπείας. Συλλογικά, αυτά τα αποτελέσματα δείχνουν πως οι ασθενείς με διαταραχές του φάσματος της σχιζοφρένειας είναι πιο ευάλωτοι στο να μολυνθούν και πιο πιθανό να πεθάνουν λόγω του COVID-19, και όμως η πρόσβασή τους σε Μονάδες Εντατικής Θεραπείας δεν φαίνεται να είναι υψηλότερη. Καταλήγουμε στο συμπέρασμα ότι οι ασθενείς με σχιζοφρένεια αποτελούν ευάλωτη ομάδα για λοίμωξη και θνησιμότητα που σχετίζεται με τον COVID-19, συνεπώς υπάρχει ανάγκη αυτή η ευάλωτη ομάδα ανθρώπων να έχει καλύτερη πρόσβαση στην υγειονομική περίθαλψη, συμπεριλαμβανομένης της προτεραιότητας σε εθνικά προγράμματα εμβολιασμού COVID-19 και καλύτερη πρόσβαση στην εντατική θεραπεία. Η μελέτη μας συνεισφέρει στην ανάγκη για ισότιμη πρόσβαση στην υγειονομική περίθαλψη για τα άτομα με διαταραχές του φάσματος της σχιζοφρένειας.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: Σχιζοφρένεια, COVID-19, θνησιμότητα, λοίμωξη, ισότητα, πρόσβαση στις υπηρεσίες, εμβολιασμός.

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