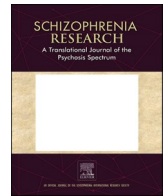




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Letter to the Editor

**Incidence and outcome of COVID-19 in patients with schizophrenia: A Study from India**

Data emerging from various parts of the globe suggest that compared to controls, patients with mental illnesses develop a more severe infection, are more likely to be hospitalized and are at a higher risk of mortality (Fond et al., 2021; Ji et al., 2020; Nemani et al., 2021; Tzur Bitan et al., 2021; Vai et al., 2021). Further, the data suggest that patients with schizophrenia are less likely to be admitted to the intensive care unit and this is attributed to the discrimination against the patients with schizophrenia (Fond et al., 2021). In terms of the type of antipsychotics available data suggests that, compared to patients on other antipsychotics, those on clozapine have a higher risk of developing COVID-19 infection (Govind et al., 2020). In terms of the risk of COVID-19 infection, data is conflicting with some of the authors suggesting a lower incidence of COVID-19 infection in patients with schizophrenia (Tzur Bitan et al., 2021), whereas others suggest a higher rate of COVID-19 infection (Wang et al., 2021). A recent systematic review which included data on risk of COVID-19-related mortality, hospitalization and intensive care unit admission rates, from different parts of the world suggests lack of data from India (Vai et al., 2021). In this background, this study aimed to evaluate the incidence of COVID-19, the need for hospitalization due to COVID-19 infection, and mortality due to COVID-19 in patients with schizophrenia. The additional aim was to understand the extent of the vaccination against COVID-19 infection among patients with schizophrenia and the incidence of COVID-19 infection in their families.

This study was conducted in a tertiary care teaching hospital in north India. The study was approved by the Institute Ethics Committee and the participants were enrolled by obtaining verbal informed consent.

At our center, prior to the onset of the pandemic, out of all the patients with schizophrenia, following up at our center, we had a list of 594 patients with a diagnosis of schizophrenia, whose contact details were available with us. A majority of these patients were on clozapine ($n = 356$) at last follow-up.

For this study, we tried to contact all these patients in the last week of June 2021 to evaluate the incidence of COVID-19 infection, the severity of COVID-19 infection, the need for hospitalization, and the outcome of COVID-19 infection in the form of mortality. During the telephonic survey, initially, the patient/caregivers were explained about the purpose of the study, their queries were addressed and verbal informed consent was obtained. The collected data was analyzed in the form of frequency, percentages, mean and standard deviation. Comparisons were made by using the Chi-square test and t -test.

Out of the 594 patients, 567 (95.45%) patients could be contacted, of whom 32 patients had developed COVID-19. Among those who developed COVID-19 infection, 23 were on clozapine alone or clozapine being one of the antipsychotic medication and 9 were on non-clozapine antipsychotics. Of those on clozapine, 12 patients developed COVID-19 infection during the first wave of COVID-19, i.e., prior to April 2021,

and remaining developed COVID-19 infection during the second wave. In the non-clozapine group, 5 developed an infection during the first wave and 4 developed the infection during the second wave.

When those who developed COVID-19 infection and those who did not develop COVID-19 infection were compared, those who developed the infection were more educated, from the urban locality, had comorbid hypertension, were on antihypertensive medication and a higher proportion of them had a family member positive for COVID-19 infection (Table 1). When the same comparisons were made for patients receiving clozapine, significant differences between those who developed and those who did not develop the COVID-19 infection were seen on the same variables as seen in the whole sample, except lack of a significant difference for locality. Whereas in the non-clozapine group, when those who developed and those who did not develop COVID-19 infection were compared, significant differences were seen only for those having a family member with COVID-19 infection, which was significantly higher among those who developed COVID-19 infection.

In terms of severity of the COVID-19 infection, 6 patients were completely asymptomatic and were detected to have infection during the routine testing for getting admitted to the psychiatry ward or receiving electroconvulsive therapy. Except for one patient, in all other patients, the COVID-19 infection was not-severe (i.e., they did not require oxygen support and the oxygen saturation did not fall below 90%), and admission was not required for the COVID-19 infection. When the sequence of infection in patients and the family members was evaluated, in 18 patients, the family members were infected before the patient, and in 8 patients, the patient was detected to be COVID-19 positive before the family member. For 3 cases, both the patient and the family members were detected to be COVID-19 positive at the same time, and in another 3 cases, only patient was infected.

When the incidence of COVID-19 infection in the family members only (but not in the patient was evaluated), 22 family members were detected to be positive for COVID-19, but the patient never developed COVID-19 infection, despite coming in contact with the family members.

Except for one patient on clozapine, whose dosage was reduced due to drug toxicity symptoms, rest of the patients continued psychotropics at prescribed dosage during the acute phase of infection.

In the whole sample, 2 patients died during the period of March 2020 to June 2021. The deaths were noted in patients who did not develop COVID-19 infection and both these patients were elderly (age > 60 years), and the cause of death was not related to any kind of infection. Based on the information provided by the family members, the cause of mortality was attributed to cardiac events in both the patients.

The present study suggests that the incidence of COVID-19 infection in patients with schizophrenia is 5.6%, with no significant difference in the incidence between those receiving clozapine and those receiving

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Table 1
Comparison of demographic and clinical variables of patients of schizophrenia those who developed and who did not develop COVID-19 infection.

Variables	COVID-19 positive group Frequency (%) or Mean (SD) N = 32	COVID-19 negative group Frequency (%) or Mean (SD) N = 535	Chi-square value/t-value (p-value)
Socio demographic			
Age (years)	38.59 (10.03)	36.68 (11.86)	−0.894 (0.372)
Education (years)	13.84 (3.15)	12.33 (4.12)	−2.2044 (0.041)*
Age group			
<45 years	24 (75.0)	409 (76.4)	0.035 (0.851)
≥45 years	8 (25.0)	126 (23.6)	
Age group			
<60 years	30 (93.8)	504 (94.2)	Y = 0.000 (1.000)
≥60 years	2 (6.2)	31 (5.8)	
Gender			
Male	14 (43.8)	314 (58.7)	2.764 (0.096)
Female	18 (56.2)	221 (41.3)	
Marriage			
Married	11 (34.4)	171 (32.0)	0.081 (0.776)
Unmarried	21 (65.6)	364 (68.0)	
Family			
Nuclear	22 (68.8)	360 (67.3)	0.029 (0.864)
Extended/joint	10 (31.2)	175 (32.7)	
Locality			
Urban	27 (84.4)	336 (62.8)	6.100 (0.014)*
Rural	5 (15.6)	199 (37.2)	
Religion			
Hindu	21 (65.6)	389 (72.7)	0.757 (0.384)
Non-Hindu	11 (34.4)	146 (27.3)	
Occupation			
Employed	9 (28.1)	105 (19.6)	1.358 (0.244)
Unemployed/Housewife	23 (71.9)	430 (80.4)	
Household income			
Less than 10,000/month	17 (53.1)	267 (49.9)	0.125 (0.724)
More than 10,000/month	15 (46.9)	268 (50.1)	
Clinical			
Age of onset of illness (years)	22.47 (7.35)	22.47 (8.28)	0.711 (0.477)
Duration of illness (months)	137.87 (92.65)	128.67 (101.35)	−0.501 (0.616)
Any comorbidity	10 (31.2)	111 (20.7)	1.984 (0.159)
Hypertension	5 (15.6)	32 (6.0)	4.604 (0.032)*
Diabetes	4 (12.5)	42 (7.9)	Y = 0.363 (0.547)
Dyslipidaemia	2 (6.2)	67 (12.5)	Y = 0.602 (0.438)
Coronary artery disease	0 (0)	3 (0.6)	FE = 1.000
Any substance use	3 (9.4)	81 (15.1)	Y = 0.404 (0.525)
Substance use type			
Smoking	2 (6.5)	63 (11.8)	Y = 0.445 (0.504)
Chewing tobacco	0 (0)	17 (3.2)	Y = 0.240 (0.624)
Alcohol use disorder	2 (6.2)	30 (5.6)	Y = 0.000 (1.000)
Last physical follow up			
Before lockdown	21 (65.6)	321 (60.0)	0.278 (0.597)
After November 2020	11 (34.4)	213 (40.0)	
Drugs			
Antipsychotic			
Clozapine	23 (71.9)	317 (59.3)	2.004 (0.157)
Non- clozapine	9 (28.1)	218 (40.7)	
Number of antipsychotics			
One antipsychotic	28 (87.5)	496 (92.7)	Y = 0.544 (0.461)
More than one antipsychotic	4 (12.5)	39 (7.3)	
Antidepressant use			
Yes	10 (31.2)	135 (25.2)	0.574 (0.449)
No	22 (68.8)	400 (74.8)	
Mood stabilizer use			
Yes	2 (6.2)	27 (5.0)	Y = 0.000 (1.000)
No	30 (93.8)	508 (95.0)	
Antihypertensive use			
Yes	5 (15.6)	32 (6.0)	4.604 (0.032)*
No	27 (84.4)	503 (94.0)	
Antidiabetic use			
Yes	4 (12.5)	42 (7.9)	Y = 0.363 (0.547)
No	28 (87.5)	493 (92.1)	
Antilipidemic drug use			
Yes	2 (6.2)	67 (12.5)	Y = 0.602 (0.438)
No	30 (93.8)	468 (87.5)	
Number of medications	1.94 (0.17)	1.87 (1.0)	−0.365 (0.715)
Adherence in last year			
100%	28 (87.5)	457 (85.4)	Y = 0.004 (0.947)
Less than 100%	4 (12.5)	78 (14.6)	
Adherence in last month			

(continued on next page)

Table 1 (continued)

Variables	COVID-19 positive group Frequency (%) or Mean (SD) N = 32	COVID-19 negative group Frequency (%) or Mean (SD) N = 535	Chi-square value/t-value (p-value)
100%	30 (93.8)	490 (91.6)	Y = 0.010 (0.920)
Less than 100%	2 (6.2)	45 (8.4)	
COVID-19			
Status of COVID-19 vaccination prior to COVID-19 positive status			
At least 1 dose	1 (3.1)	–	–
Not vaccinated	31 (96.9)	–	–
COVID-19 positive in family member	18 (56.2)	22 (4.1)	117.351 (0.001)***

other antipsychotic medications. According to an estimate, population of India is 1,394,528, 165 and the number of COVID-19 cases in India is 31,219, 374 (as of third week of July 2021). Accordingly, the incidence of COVID-19 in the country is about 2.23%. When we compare the incidence findings of COVID-19 infection of the present study with this data, it can be said that the incidence of COVID-19 in patients with schizophrenia is higher than the general population. It is important to note that this is a crude way to compare the figures, but this was done, as the breakup of incidence of COVID-19 in different age-groups in India was not available. This finding of higher incidence of COVID-19 in patients with schizophrenia is similar to the findings reported from China (Wang et al., 2021).

In terms of severity of COVID-19 infection, our data contradicts the findings from other countries, which have reported that patients with schizophrenia are more likely to be hospitalized and are at a higher risk of mortality (Vai et al., 2021). The lower hospitalization rates in the present study could be argued to be due to the lack of availability of facilities, especially during the second wave of the infection. However, this appears to be less likely because, in the majority of the patients, the infection was not severe enough to require hospitalization. Our findings also contradict the finding from the United Kingdom, which suggest that compared to other antipsychotics, patients on clozapine are at higher risk of developing COVID-19 infection (Govind et al., 2020).

It is important to note that the incidence of psychosis in patients with various viral infections varies from 0.9 to 4% (Brown et al., 2020). Accordingly, it can be said that there is a bilateral interaction between psychosis and various viral infections. Hence, in the ongoing pandemic, clinicians managing both new and old patients with psychosis should enquire about the history of COVID-19 infection.

Our study has certain limitations, which included small sample size and a lack of a control group.

To conclude, the present study suggests that the incidence of COVID-19 infection in patients with schizophrenia is 5.6%, which appears to be higher than that seen in the general population. There was no significant difference in the incidence of COVID-19 between those receiving clozapine and those receiving other antipsychotic medications. In the majority of the patients with schizophrenia, the COVID-19 infection was not severe, and the majority of the patients did not require oxygen support and hospitalization. The majority of the patients also did not require a change in the doses of psychotropic medications during the acute phase of COVID-19 infection.

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CRedit authorship contribution statement

SG: Concept, drafting of the manuscript, collection of data, analysis of data, final approval of the manuscript.

SK: Concept, drafting of the manuscript, collection of data, analysis of data, final approval of the manuscript.

AS: Concept, drafting of the manuscript, collection of data, final approval of the manuscript.

CN: Concept, collection of data, final approval of the manuscript.

AM: Concept, final approval of the manuscript.

SS: Concept, final approval of the manuscript.

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Declaration of competing interest

None.

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