Study of the Prevalence of COVID-19 Infection among Patients on Antidepressants: A Cross Sectional Study in A Tertiary Care Hospital

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Abstract:

Context: With growing evidence supporting the beneficial role of antidepressants in improving the prognosis of COVID-19 infection, and possibly even prevent infection, this study was taken up in the outpatient setting.

Aim: Our goal was to assess the prevalence of COVID-19 infection among patients on antidepressants, and to compare it with that in the control group along with illness and treatment variables.

Settings and Design: 50 patients attending Psychiatric Department, SVRRGGH, Tirupathi (tertiary care centre) who were on regular antidepressant medication for a minimum of 3 years (3 months at time of any reported COVID-19 infection) were evaluated as the antidepressant group, along with their corresponding informants as the control group who were not on any psychotropic drug at any point of time.

Material& Methods: This was done as a hospital based cross-sectional study on the antidepressant and control group as defined above. Each subject was administered a semi structured questionnaire including details of socio-demographic variables, specific details regarding history of COVID-19 infection, its course, vaccination status.

Statistical analysis used: The data was analysed using Chi-square test and t-test.

Results: 12% of those in the antidepressant group had a history of COVID-19 infection as opposed to 16% of those from the control group (confirmed via a positive RT-PCR report).

Conclusions: According to the study's findings, the prevalence COVID-19 infection was found to be more in the control group, than in those on antidepressants.

Keywords: COVID-19 Infection, Antidepressant, Vaccination.

Introduction

This study was taken up in the wake of growing evidence that antidepressants have a beneficial role in improving the prognosis of COVID-19 infection, and possibly even prevent infection.

This study is an attempt to explore the association of antidepressant use including SSRI's as well as TCA's and correlates their usage with the prevalence and severity of COVID-19 infection. There is much scope for research in this particular domain, the results of which could greatly aid in repurposing existing drugs for COVID-19 treatment protocol and even possible prevention strategies.

Aim: The aim was to assess the prevalence of COVID-19 infection among patients on antidepressants.

Objectives:

- To compare the prevalence of COVID-19 infection among patients on antidepressants with that in the control group.
- To compare the prevalence of COVID-19 infection among patients on antidepressants, with illness and treatment variables.

Subjects and Methods

This study was carried out at the Psychiatric Department, SVRRGGH, Tirupathi (tertiary care centre). The Institutional Ethical Committee gave its approval to the study. The study population comprised individuals aged between 18-60 yrs and was divided into two groups. 50 patients attending Psychiatric Department, SVRRGGH, Tirupathi (tertiary care centre) who were on regular antidepressant medication for a minimum of 3 years (3

months at time of any reported COVID-19 infection) were evaluated as the antidepressant group. For the control group, one informant of each subject in the antidepressant group was taken, who had not been on any psychotropic drug at any point of time. The study excluded patients with chronic debilitating conditions such as congestive heart failure, chronic hepatic failure, chronic renal failure, carcinomas, and those on immunomodulator drugs.

Procedure: The participants were explained about the nature of the study, and written informed consent was obtained. The socio-demographic and clinical information were recorded. All the patients were administered a semi-structured questionnaire including details of socio-demographic variables and specific details such as history of COVID-19 infection, its course, and vaccination status.

Statistical analysis: The data was entered into MS Excel 2007 version

- Descriptive statistics were analyzed as follows: The categorical data was analyzed using percentages and the continuous data was analyzed using mean and standard deviation.
- Inferential statistics were analyzed using Chi-square test and t-test
- Confidence interval was set at 95% and a probability value of $p < 0.05$ was considered as statistically significant.

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) V.25.0.

Results:

a) Socio-demographic data: (Fig 1): This study was conducted on 50 subjects each in the antidepressant group and control group. The study population comprised of 44 males and 56 females. 88% of them were found to be married. 90% were Hindus and the remaining 10 Muslims. Slightly more from nuclear families (55%) than joint families (45%), with those from urban background (56%) exceeding those from rural background (44%).

Majority of the study population belonged to a lower socio-economic status (68%), with the remaining distributed between lower middle (24%) and upper middle (8%) socio-economic status based on the modified Kuppuswamy scale.

b) Clinical data: Prevalence of COVID-19 infection (Table 1) - Analysis of clinical data showed that In the current study population, 16% of those from the control group and 12% of their counterparts in the antidepressant group had a history of COVID-19 infection (confirmed via a positive RT-PCR report).

The prevalence is thus more in the control group. Vaccination and illness variables (Table 2) - Among the study participants, five from the antidepressant group, and three from the control group completed their vaccination schedule.

Of those with previous COVID-19 infection, hospitalization was required in four from the control group as opposed to three from the antidepressant group.

Oxygen supplementation was given for four from the control group, but in only one from the antidepressant group. One from the control group reported more than 1 episode of COVID-19 infection, with none from the antidepressant group.

Based on the above studied illness variables, more severity of COVID-19 infection was seen in control group.
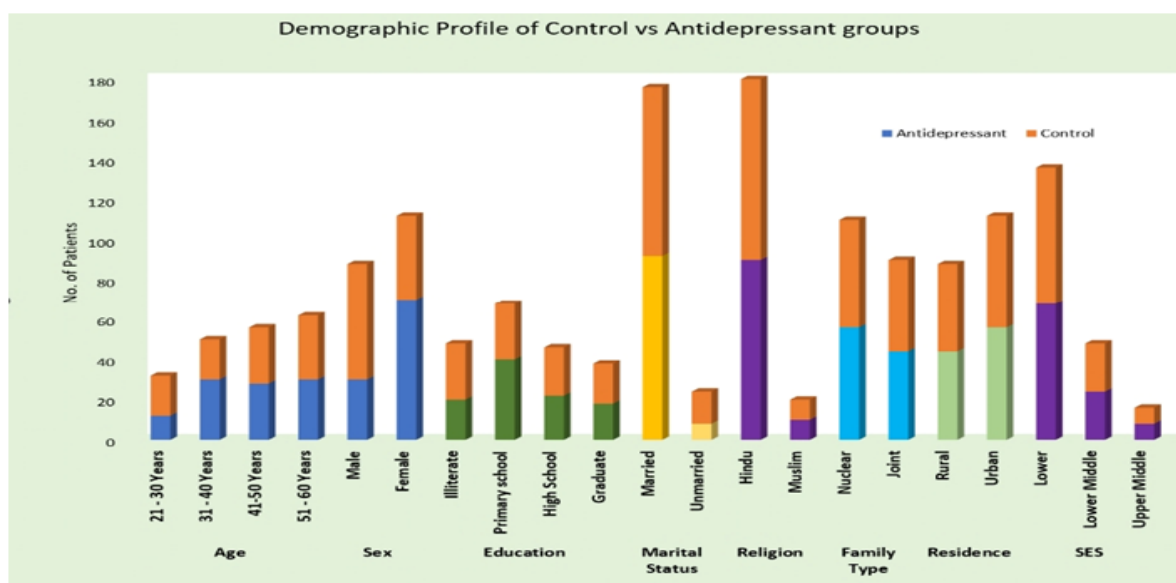

Figure 1: Demographic profile

Table 1: Prevalence of COVID-19 infection in Antidepressant group vs Control group

RTPCR	Group						Chi-square
	Anti-depressant		Control		Total		
	F	%	F	%	F	%	
Yes	6	12.0	8	16.0	14	14.0	$\chi2 = 0.332^{@}$; (p = 0.564) df= 1;
No	44	88.0	42	84.0	86	86.0	
Total	50	100.0	50	100.0	100	100.0	

Table 2: Comparison of vaccination and treatment variables in antidepressant and control groups

		Group			Sig.
		Antidepressant	Control	Total	
No of Vaccination Doses	No Dose	9	8	17	
	First Dose	1	5	6	P > 0.05
	Second Dose	35	34	69	
	Third Dose	5	3	8	
	Total	**50**	**50**	**100**	
Hospitalization	Yes	3	4	7	P > 0.05
	No	3	4	7	
	Total	**6**	**8**	**14**	
Oxygen	Yes	1	4	5	P > 0.05
	No	5	2	7	
	Total	**6**	**6**	**12**	
Morethan1Episode	Yes	0	1	1	P > 0.05
	No	6	6	12	
	Total	**6**	**7**	**13**	

Discussion

The present investigation was a hospital based cross sectional study comprising individuals aged between 18-60 yrs, in 50 subjects on antidepressants and 50 individuals as control.

Some of the relevant study findings are as follows- Preventive effects of common psychotropic drugs have been suggested against SARS- COV-2 infection adverse outcomes.[1] There is strong retrospective evidence of decrease in death rates with SSRI's (particularly with Fluvoxamine and Fluoxetine). Fluoxamine was found to be a sigma 1 receptor (S1R) agonist, with properties said to interrupt viral replication and prevent hyper inflammation.[2] SSRIs in general were found to have antiviral properties, and to decrease pro-inflammatory cytokines.[3] Studies have also shown that some antidepressants may inhibit cell entry of SARS-COV-2 via inhibition of the acid sphingomyelinase (ASM)/ceramide system, which is likely required to facilitate ACE2 binding of the SARS-CoV-2 virus.[4]

Prevalence of COVID-19 infection- In this study, the prevalence was more in control group (16%) than the antidepressant group (12%). This is in accordance with other literature as mentioned. Antidepressants were shown to reduce coronavirus infection rates as patients who were receiving these medications were less likely to test positive for COVID-19. (Mainly SSRIs) (Clelland C.L et al) [5] A significant protective association was observed between antidepressant use and COVID-19 infection (SSRI, SNRI, SARI) Some SSRI antidepressants, such as fluvoxamine which is a functional inhibitor of acid sphingomyelinase activity (FI-ASMA), may prevent the infection of epithelial cells with SARS-CoV-2. (Gulbins E., et al)[6]

Severity of illness variables- More participants from the control group had history of hospitalization, oxygen supplementation and multiple episodes in relation to COVID-19 infection. These findings too were in accordance to several other mentioned studies. In a systematic review by Nakhaee H et al, eight out of 14 articles showed effect of antidepressants on reducing severity of COVID-19 infection.[7]

Treatment of Depression as an underlying morbidity was found to decrease the risk of clinical deterioration in Covid-19 patients. (since clinical depression was associated with lower immunity levels) (Das A., et al 2021)[8]. Antidepressants are also associated with less severe cases as they significantly reduced the risk of intubation or death in some cohort studies (Hoertel N et al.)[9], (Diez-Quevedo C et al)[10]. They can also act by improving psychosocial risk factors well known to be relevant to prognosis for patients with medical conditions such as psychosocial stress and insomnia. (Diez-Quevedo C et al)[10]

Limitations of study: The main limitation of this study was the small size of the patient sample investigated. Study patients were those attending a tertiary hospital facility, so they may not be representative of the total COVID-19 patient

population. The analyses were done retrospectively which might have added to recall bias. Also, the associations observed were found in a non-randomized sample, so they do not imply a cause-effect relationship. Further, confounders were not adequately accounted for (including vaccination status, other medications, any missed or subclinical infection, availability of treatment, comorbidities).

Conclusion

These possible beneficial effects found with antidepressants may become particularly salient for in-patient settings if vaccine-resistant strains of the virus appear. The ultimate triumph would be to develop cost effective, easily accessible medication-based COVID-19 prevention strategies for the future. There is definitely a need for further study in this area, particularly in the Indian context.

Future directions: A follow-up larger study that also evaluates characteristics of COVID-19 infection would be beneficial to confirm these findings. Further clinical trials should be conducted to clarify the effects of antidepressants on the severity of COVID-19 (whether biological- directs antiviral as well as immunoprotective, psychosocial, or possibly other mechanisms as well.

Further study is required to compare effects of each class of antidepressants, as currently only SSRI's have been majorly studied, with few studies on SNRI's. Based on the specific wave of COVID-19 infection, differences in effects on specific strains could be explored, however the retrospective nature would be a limitation.

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