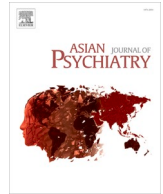




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Relationship of substance dependence and time to RT-PCR negative status in patients with COVID-19 infection

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ARTICLE INFO

Keywords:

Substance abuse
COVID-19
Association
Outcome

ABSTRACT

Background: To date, no study has evaluated the association of alcohol dependence with the outcome of the COVID-19 infection.

Aim: The current study aimed to evaluate the association of substance dependence (alcohol and tobacco) with the outcome (i.e., time to have two consecutive negative test reports) of the COVID-19 infection.

Results: The mean age of the study participants (n = 95) was 37.2 yrs (SD-13.2). More than half of the participants were males. About one-fourth (N = 25; 26.3 %) were consuming various substances in a dependent pattern. Alcohol dependence was present in 21 participants (22.1 %), and Tobacco dependence was present in 10.5 % of participants. Even after using gender, age, and physical illness as covariates, patients with any kind of substance dependence had a significantly lower chance of having a negative report on RT-PCR on 14th day, 18th 23rd day.

Conclusion: Persons with substance dependence takes a longer time to test negative on RT-PCR, once diagnosed with COVID-19 infection. Mental health professionals involved in the care of patients with COVID-19 should accordingly prepare these patients for a possible longer hospital stay to reduce the distress associated with prolongation of hospital stay.

1. Introduction

Since the declaration of COVID-19 as a pandemic, the number of cases of COVID-19 increased rapidly across the globe in devastating numbers, and it resulted in numerous psychosocial problems (Tandon, 2020). With the emergence of data, there is some understanding of the prognostic factors associated with poor outcome and mortality. Some of the factors which are associated with a poor outcome include age more than 65 yrs, presence of hypertension (Pranata et al., 2020), chronic obstructive pulmonary disease (COPD) (Alqahtani et al., 2020), diabetes mellitus (Huang et al., 2020), abnormal blood parameters such as leukocytosis, neutrophilia, high troponin I levels, smoking, and presence of other physical illnesses (Hu et al., 2020).

Available data suggest that compared to non-smokers, smoker are at a high risk of developing COVID-19 and being smoker is also associated with higher risk of COVID-19 related mortality (Salah et al., 2020). Some data suggest that smoking is associated with poor outcome and

late recovery among patients with COVID-19 infection. In a recent systematic review, it was reported that smokers have 1.4 times higher risk of having severe symptoms of COVID-19 and 2.4 times higher risk of admission to ICU, need for mechanical ventilation, and die when compared to non-smokers (Vardavas and Nikitara, 2020). Systematic reviews suggest association of the severity of COVID-19 and smoking (Zhao et al., 2020; Izcovich et al., 2020).

It is also suggested that alcohol consumption is associated with higher risk (7–8 times higher risk) of developing respiratory infection and having higher severity of respiratory bacterial infections (Fernández-Solá et al., 1995; Happel and Nelson, 2005; MacGregor and Louria, 1997). Chronic alcohol consumption has also been linked to a higher risk of severe influenza virus infections by altering the immune response (Meyerholz et al., 2008). But to date, no study has evaluated the association of alcohol with the COVID-19 disease's severity, progression or outcome of the illness.

Although some studies have evaluated the association of smoking

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<https://doi.org/10.1016/j.ajp.2021.102562>

Received 21 October 2020; Received in revised form 10 January 2021; Accepted 18 January 2021

Available online 21 January 2021

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with the outcome of the COVID-19 (Vardavas and Nikitara, 2020), to date, no study has assessed the association of alcohol with outcome of the COVID-19. In this background, this study aimed to evaluate the association of substance dependence with the outcome [i.e., time to have 2 consecutive negative reverse transcriptase-polymerase chain reaction (RT-PCR) oro-pharyngeal test reports] of the COVID-19 infection.

2. Material and methodology

It was a retrospective study conducted at a tertiary care center. The institute ethics committee approved the study.

Data of patients admitted in the designated COVID-19 ward during the period of 1st April-15th May 2020 was extracted. The COVID ward is designated only for the patients who are found to be positive for COVID-19 infection on RT-PCR assay of oropharyngeal swab specimens. The diagnosis was based on the diagnosis of the interim guidelines of the World Health Organization (WHO, 2020). At the time of admission to the COVID ward, all the patients undergo detailed evaluation for the presence of various physical illnesses. They also underwent a comprehensive psychiatric evaluation by a qualified psychiatrist to assess for any kind of psychiatric morbidity, including substance dependence, according to the International Classification of Diseases, Tenth Revision (ICD-10) criteria, using a semi-structured interview. The psychiatric evaluation of patients was done by a consultant psychiatrist through video conferencing, by using a semi-structured interview, to evaluate the presence of any psychiatric diagnosis, psychiatry symptoms and substance use. If any patient was detected to be using the substance, they are evaluated for withdrawal symptoms and these are managed using appropriate pharmacological and non-pharmacological measures. Further the patients were regularly counselled/managed by the psychiatrist on a regular basis by the same psychiatrist through video conferencing. The psychiatrist's contact number was also provided to the patients so that they could contact the psychiatrist at the time of crisis. The information about the psychiatric history and physical comorbidity is also corroborated from the family members telephonically. During the hospital stay, patients were clinically monitored and managed symptomatically. On 14th day, a repeat RT-PCR test was done for asymptomatic patients, and if the RT-PCR report came out negative twice in a 24 h interval, these patients are considered to have recovered and are discharged from the hospital. Those patients who do not test negative on RT-PCR twice at 24 -h intervals undergo repeat RT-PCR tests every 4th day, i.e., on 18th day and 22nd day, and so on.

For this study, data of all the patients diagnosed with COVID-19 infection and those aged ≥ 18 years were extracted. During the study period, 98 patients aged ≥ 18 years were admitted to the COVID-19, of whom details of substance abuse were available for 95 patients. Three patients were directly admitted to the intensive care unit; hence they were not evaluated by the psychiatrist at the time of admission. They expired before further evaluation for substance dependence and psychiatric morbidity. All the 95 patients were clinically asymptomatic and stable at the baseline assessment. The socio-demographic information, such as age, sex, marital status, socioeconomic status, was extracted. Data of blood investigation including complete blood count, Liver function test, Renal function test, D-dimer, Chest x-ray PA view was also extracted. Physical morbidity details were also extracted from the treatment records.

In the present study, outcomes were evaluated in the form of time to RT-PCR negative status in addition to being symptom free from the COVID-19 infection.

3. Statistical analysis

Chi-square test or Fischer's exact test were used for categorical variables. For continuous variables, mean and standard deviation were calculated. Comparisons were made by using the Student *t*-test or Mann-Whitney test. Associations between various variables were studied by

using Pearson coefficient-correlation. All *p* values were two-sided, and *p* values of < 0.05 were considered statistically significant.

4. Results

The mean age of the study participants ($n = 95$) was 37.2 yrs (SD-13.2). More than half of the participants were male and from lower socioeconomic status. About three fourth were married.

About one-fourth ($n = 25$; 26.3 %) were consuming substances in a dependent pattern, of whom 7 were taking more than 1 substance, and 18 were using only one substance (Table 1). Alcohol dependence was present in 21 participants (22.1 %). Tobacco dependence was present in 10.5 % of cases. The details of physical morbidity and abnormal level of parameters on investigations are depicted in Table 1.

On 14th Day, i.e. after 2 weeks of baseline assessment, about one third (35.8 %) of patients were found to be negative on RT-PCR. This percentage increased to 46.3 % and 49.5 % by day 18 and day 23rd, respectively.

When those with any substance dependence and those without substance dependence were compared, it was seen that a significantly lower proportion of the patients with substance dependence tested negative on RT-PCR on 14th day, 18th day, and 23rd day. Among the substance users, a significantly higher proportion of them were males. Hence, gender, age, and presence of physical illness were used as a covariate, but the statistical significance persisted for all the 3 assessments (Table 2).

When the same analysis was carried out by comparing those with alcohol dependence only ($n = 21$) with those without any substance dependence ($n = 70$), similar results were replicated and persisted even after controlling for gender. When a similar analysis was done for those with tobacco dependence ($n = 10$) and those without any substance dependence ($n = 70$), the same results were replicated. The presence of physical illness had no correlation with the reporting status of RT-PCR on any day.

5. Discussion

As per WHO, drinking alcohol, and smoking are associated with a

Table 1
Sociodemographic and clinic profile.

Variables	Frequency (%)/ Mean (SD) (n = 95)
Age	37.2 (13.2); Range :18–67
Gender : Male /Female	57 (60.0 %)/38 (40.0 %)
Marital status : Married /Single	69 (72.6 %)/26 (27.4 %)
Socio-economic status	
Lower	48 (50.5 %)
Middle	37 (38.9 %)
Upper	10 (10.5 %)
Clinic profile of substance use	
Substance dependence and actively using before admission	
Present	25 (26.3 %)
Absent	70 (73.7 %)
More than 1 substances use - present	7 (7.4 %)
Alcohol dependence	21 (22.1 %)
Tobacco dependence	10 (10.5 %)
Physical morbidity	
Hypertension	9 (9.5 %)
Hypothyroidism	4 (4.2 %)
Diabetes mellitus	10 (10.5 %)
HIV/AIDS	1 (1.1 %)
One physical morbidity	18 (18.4 %)
More than >1 Physical illness	4 (4.2 %)
Abnormal Laboratory investigation	
Anemia	4 (4.2 %)
Abnormal D-Dimer	31 (32.6 %)
Thrombocytopenia	4 (4.2 %)

Table 2
Comparison between substance users and non-substance.

Variables	Substance users (n = 25)	Non-substance users (n = 70)	Chi-square value(p-value)	ANCOVA [#]
Status of the patient on the 14 th day (COVID-19)				
Positive	22 (88.0 %)	39 (55.7 %)	8.356	F-4.436
Negative	3 (12.0 %)	31 (44.3 %)	(0.004**)	(0.014*)
Status of the patient on the 18 th day (COVID-19)				
Positive	19 (76.0 %)	32 (45.7 %)	6.795	F-3.580
Negative	6 (24.0 %)	38 (54.3 %)	(0.009**)	(0.032*)
Status of the patient on the 23 rd day (COVID-19)				
Positive	18 (72.0 %)	30 (40.0 %)	6.259	F-3.245
Negative	7 (28.0 %)	40 (60.0 %)	(0.012**)	(0.043*)

Age was used as the covariate.

more complicated and dangerous progression of COVID-19 (World Health Organization, 2020). However, little is known about how the use of substances influences patients' testing status with COVID-19 infection. The present study shows that those who were using any substance, tobacco only, and alcohol only took a long time to test negative on RT-PCR compared to those who were not taking any substances. These findings provide evidence for the negative impact of substance dependence on COVID-19 status. These findings can have significant clinical implications in the form of educating the public about the risk of prolonged stay for these patients in the COVID wards.

These findings can have severe implications for people with pre-existing mental illnesses, who often have high substance dependence rates. Accordingly, mental health professionals need to emphasize this fact to their patients and prepare them for a relatively lengthy hospital stay, compared to patients who do not use any kind of substance. Further, the mental health professionals need to manage withdrawal from these substances in patients admitted to COVID wards. At present, it is difficult to say why these patients take a longer time to test negative. Future research must attempt to assess the same.

The present study has certain limitations, in the form of retrospective study design, small sample size, and inclusion of data of only less serious patients. We did not evaluate the exact amount of the substances used before being diagnosed with COVID-19 infection. The other confounding factors, like the duration of symptoms, were not taken into account because all the patients were asymptomatic at the time of testing and were tested because of the contact history. Further, the method of sample collection and sensitivity and specificity of RT-PCR should not be ignored while interpreting our study's findings.

To conclude, the present study suggests that patients with substance dependence take a longer time to test negative on RT-PCR, once diagnosed with COVID-19 infection. Mental health professionals involved in the care of patients with COVID-19 should accordingly prepare these patients for a possible longer hospital stay, as last-minute disclosure of prolongation of hospital stay can lead to significant distress to the

patients who are staying in isolation with an expectation of discharge by 2 weeks time.

Financial Disclosures/ funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

All authors have no conflicts of interest to declare.

Acknowledgements

We sincerely acknowledge the contribution of all the health care professionals involved in the care of the patients with COVID-19 admitted at Nehru Extension Block, Postgraduate Institute of Medical Education and Research, Chandigarh

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