Cognitive Deficits in Patients with COVID-19 Infection during Their Hospital Stay: An Exploratory Study

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Abstract

Background The literature on presence of cognitive deficits in patients recovered from coronavirus disease 2019 (COVID-19) infection is emerging. However, the data on whether cognitive deficits have its onset during the acute phase of illness has not been evaluated extensively.

Aim This article estimates the level of cognitive functioning of patients with COVID-19 while they were admitted to COVID-designated wards. Secondary objectives were to assess the influence of medical comorbidities, severity of COVID-19 infection, and depressive and anxiety symptoms on cognitive functioning in patients with COVID-19 infection.

Methods Sixty-six clinically stable patients with COVID-19 infection were evaluated during their inpatient stay on Hindi Montreal Cognitive Assessment scale (H-MoCA), Hindi Mini-Mental State Examination (HMSE) scale, Patient Health Questionnaire-9, and Generalized Anxiety Disorder Questionnaire -7.

Results The mean age of the study participants was 39.85 (standard deviation [SD] 16.89) years and the participants were evaluated after 9.34 (SD 4.98; median 9.0) days of being diagnosed with COVID-19 infection. About one-fourth (28.8%; $n = 19$) of the participants had cognitive impairment on HMSE and about two-fifths ($n = 26$; 39.39%) had cognitive impairment as per the cutoff used for H-MoCA. A higher level of cognitive deficits were seen among participants who were older, diagnosed with diabetes mellitus, and those who required oxygen support during their hospital stay prior to assessment.

Conclusion Low cognitive score was found in one-fourth (28.8%) to two-fifths (39.9%) of the persons, depending on the assessment scale among those with acute COVID-19 infection. Low cognitive score was more prevalent among the elderly, those with diabetes mellitus, and those who required oxygen support prior to the assessment.

Keywords
- COVID-19
- cognitive impairment
- depression
- anxiety

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Introduction

Now it is well-known that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or coronavirus disease 2019 (COVID-19) infection affects almost all systems of the human body. COVID-19 infection has also been found to have a plethora of neuropsychiatric symptoms due to direct impact of SARS-CoV-2 virus on the central nervous system (CNS) and/or due to the cerebral hypoxia in severe cases.[1,2]

The CNS viral infection and cerebral hypoxia can lead to cognitive impairment, which can be transient or long-lasting. Earlier epidemics of SARS and Middle East respiratory syndrome suggested an association between the viral infections with poor concentration, decline in memory, and executive dysfunctions, indicating cognitive impairment.[3] There is also existing literature which suggests there can be neurologic alterations and hypoxic brain injury associated with acute viral infections (H1N1 influenza, human respiratory syncytial virus, the human metapneumovirus, etc.).[4,5]

The studies done during the ongoing COVID-19 pandemic suggest that about one-third of the patients report neurological symptoms,[6,7] and is associated with a negative impact on the patient's cognitive functions.[8] A recent study suggest that the incidence of new neurological or psychiatric diagnosis in persons who developed COVID-19 infection was 12.84%, with the incidence being 25.79% among those admitted to the intensive therapy unit.[7] Studies have found prevalence of depression and anxiety symptoms to be approximately 61 and 45% in persons with diabetes mellitus during the COVID-19 outbreak.[9]

Recent studies which had looked into the neurocognitive performance of patients with COVID-19 infection have revealed that COVID-19 infection has negative impact on the cognitive functioning of the affected persons during the active phase of illness as well as leave a person with cognitive deficits during the recovery phase too.[10,11] The prevalence of cognitive impairment in different studies have been reported to range from 34 to 81%[10,11] and deficits were noted in the domains of working memory, set-shifting, divided attention, and processing speed. One study reported potential relationship between attentional deficits and serum C-reactive protein (CRP) levels suggesting the possible role of the underlying inflammatory processes.[12]

Still, the existing literature on the cognitive deficits in patients with COVID-19 infection is limited. The available studies had limited sample size (ranging from 29 to 50 patients), were mostly done in recovered patients, and several factors (such as age, requirement of respiratory support, severity of illness, presence of pneumonia, comorbidities, presence of anxiety and depressive symptoms) could have affected the cognitive profile adversely, which have not been taken into account consistently.[10–13]

In this regard, it is essential to estimate the cognitive scores during the active phase of illness, so as to identify the subjects who are prone to develop significant cognitive deficits later on and thereby plan early interventions for improving cognitions during recovery period. This can ultimately hasten the recovery process altogether and possibly prevent the long-term cognitive impairment. In this background, the current study aimed to estimate the cognitive functioning of patients with COVID-19 while they were admitted to COVID-designated wards. Secondary objectives were to assess the influence of medical comorbidities, severity of COVID-19 infection, and depressive and anxiety symptoms on cognitive functioning in patients with COVID-19 infection.

Methods

At our setting, patients (age > 18 years) with confirmed COVID-19 infection (i.e., positive reverse transcriptase polymerase chain reaction [RT-PCR] assay of nasal/oropharyngeal swabs), are admitted at designated COVID-19 set up. On the first day of admission these patients are evaluated in detail for the physical comorbidities and mental disorders. The patients were telephonically interviewed (using video conferencing through WhatsApp video calling facility or voice calling) by a mental health professionals (who are part of the core COVID-19 management team of the hospital) at the baseline for assessment of any mental health issues.[14] This assessment focuses on any present or past psychiatric disorder, any ongoing mental issues, and substance use disorders. The information provided is also corroborated from the family members telephonically. The severity of COVID infection was decided by the medicine treating team based on symptoms, need for oxygen, comorbidities, and computed tomography (CT) chest scan findings.

This was a prospective study in which participants were assessed once. To be included in the study, the participants were required to have COVID-19 infection confirmed by RT-PCR test, admitted to the COVID hospital, aged > 18 years, of either gender, providing verbal informed consent, cooperative for assessment, and hemodynamically stable. Patients who refused to provide consent for participation, those who had active hyperthermia (fever > 99°F), those on oxygen requirement during the time of assessment, those who were uncooperative, and clinically unstable were excluded. Similarly, patients currently in delirium or those who had history of delirium in 3 days prior to assessment were excluded. Persons diagnosed with dementia and any other psychiatric disorders were excluded.

Neurocognitive assessment was done on the eligible participants by a psychiatry trainee resident in-person, while undertaking all COVID protocol and safety measures (i.e., in personal protective equipment for COVID). Data on patient's demographic data, clinical profile, and medical history were collected from the available treatment records. Anxiety and depressive symptoms were assessed by Generalized Anxiety Disorder Questionnaire-7 (GAD-7)[15] and Patient Health Questionnaire-9 (PHQ-9),[16] respectively. Cognitive assessment was done by using the Hindi translated version of the original Montreal Cognitive Assessment (H-MoCA)[17,18] and Hindi Mental Status Examination (HMSE).[19,20]

MoCA, a brief 30-item questionnaire assesses attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking,

calculations, and orientation (total score of 30 and a score of ≥ 26 is considered normal). For the study, we had used the H-MoCA scale which have been validated in previous studies.[17] The cutoff score of 26 has been kept according to the norms established in the validation study of the H-MoCA instrument.[17] The HMSE, a modified version of Mini-Mental State Examination (MMSE), is designed mainly for illiterate Hindi speaking population with a less emphasis on calculation ability[20] (HMSE scores ≤ 25 can be considered "cognitively impaired"). Both the scales has been validated in Hindi speaking illiterate and literate participants.[17,20]

The study was approved by the Institute's Ethics committee. The data was analyzed using SPSS software, version 20.0. Descriptive statistics were applied. Pearson's correlation coefficient, chi-square test, and independent *t*-test were used to finding the association between different variables. Bonferroni correction was applied to address multiple comparisons, and $p = 0.001$ (0.05/45) was considered statistically significant.

Results

During the study period (November–December 2020), a total of 66 participants were enrolled into the study.

The mean age of the study participants was 39.85 (standard deviation [SD] 16.89; range 20–79; median: 31.5) years. About one-eight ($n = 8$; 12%) of the participants were aged > 65 years. Majority of the participants were male ($n = 40$; 60.6%), married ($n = 40$; 60.6%), and employed (66.7%) at the time of admission. The mean year of education of the sample was 13.4 ($\pm$ 1.31) years. The mean difference between the date of RT-PCR positivity and date of cognitive assessment was 9.34 (SD 4.98; range 2–29; median 9.0) days, that is, all were in the active phase of illness, were clinically stable, and cooperative.

About one-fifth were diagnosed with hypertension ($n = 13$; 19.7%) and diabetes mellitus ($n = 13$; 19.7%); and slightly more than one-fourth ($n = 19$; 28.8%) had at least one chronic physical illness (►**Table 1**). One-fifth ($n = 14$; 21.1%) had more than one physical illness. Majority of the patients had mild ($n = 35$; 53.0%) infection or were asymptomatic ($n = 17$; 25.8%). Majority of patients who were asymptomatic or had mild symptoms, were our hospital staff (doctors and nursing staff) who had to be admitted due to difficulties related to self-isolation, and had to be admitted as per the hospital policy.

Only one-eight (13%) of the participants had severe COVID-19 infection. Most common reason for admission was fever ($n = 18$; 27.2%) followed by breathlessness/breathing difficulties (24.2%) and being a health care worker (unable to self-isolate) (24.2%). About two-fifths of the participants ($n = 26$; 39.4%) required oxygen support (either through nasal prongs or venturi mask) anytime during their hospital stay, prior to their assessment. About 7.6% ($n = 5$) had a history of delirium during the current admission prior to the date of evaluation (i.e., recovered from COVID-19 delirium) (►**Table 1**).

Cognitive Profile of Patients with COVID-19 Infection as per HMSE and H-MoCA

As per the established cutoffs of HMSE, 28.8% ($n = 19$) of the participants had cognitive impairment (►**Table 2**). On H-MoCA, about two-fifths had cognitive impairment ($n = 26$; 39.39%). One-fourth ($n = 17$; 25.8%) of the participants could be categorized as having low cognitive scores as per both HMSE and H-MoCA. About one-eight (12%) of the participants could be better categorized as having cognitive impairment by MoCA but not by HMSE (►**Table 2**).

Anxiety and Depression Symptoms during the Hospital Stay

Anxiety symptoms (GAD-7 score ≥ 5) were found in approximately 45.5% of patients, with moderate to severe anxiety symptoms (GAD-7score $\geq$ 10) noted in about one-fifth (19.7%) of the participants. Depressive symptoms were reported by more than two-fifths of the patients (43.9%). In total, 16.7% of the participants screened positive for both anxiety and depression (►**Table 3**).

Relationship of MMSE and H-MoCA Domains with Clinical Parameters

When the relationship of HMSE and H-MoCA with age and clinical profile was evaluated, low cognitive scores were noted in people with higher age (►**Table 4**). When the association of total HMSE score and total H-MoCA score was evaluated, significant positive association was noted between the two scales (Pearson's corelation coefficient value r 0.927; $p < 0.001$).

When those with and without cognitive impairment as per HMSE were compared, it was noted that those with low cognitive score were significantly older, were more often married, and had required oxygen support during their hospital stay (►**Table 5**). Similarly, when those with and without cognitive impairment/low score as per H-MoCA were compared, significant differences were noted on age, presence of diabetes mellitus, and those requiring oxygen (►**Table 6**). Additionally, it was seen that compared with those without cognitive impairment, significantly higher proportion of those with cognitive impairment had severe infection (►**Table 6**).

Discussion

The present study attempted to explore the neurocognitive deficits in persons with COVID-19 infection during the acute phase of infection. We used two scales for evaluating cognitive profile (HMSE and H-MoCA) so as to have a broader picture of the neurocognitive profile.

The present study evaluated 66 stable patients on their 9th median day of RT-PCR positivity. The clinical profile of the participants included in the present study is almost similar to the clinical profile of patients with COVID-19 infection admitted to our set up[21] and other parts of India[22,23] and World.[24,25]

With regard to the cognitive profile approximately 30% of patients had cognitive impairment as per HMSE and 40% of

Table 1 Demographic and clinical details ($n = 66$)

Variables	Frequency (%)/Mean (SD) ($n = 66$)
Age	39.85 (16.89); range:18–79 Median: 31.5
Age $\geq$ 65 y	8 (12.1%)
Gender: Male/Female	40 (60.6%)/26 (39.4%)
Education (in y)	13.40 ($\pm$ 1.31)
Marital status: Married/Single	40 (60.6%)/26 (39.4%)
Employment: Employed/Unemployed	44 (66.7%)/22 (33.3%)
Religion: Hindu/Non-Hindu	47 (71.2%)/19 (28.8%)
Family type: Nuclear/Nonnuclear	49 (74.2%)/17 (25.8%)
Difference between date of RT-PCR positive and date of cognitive evaluation (in d)	9.34 (4.98); Range: 2–29 Median: 9.0
Comorbid conditions	
Hypertension	13 (19.7%)
Diabetes mellitus	13 (19.7%)
Diabetes mellitus with organ damage	1 (1.5%)
Congestive cardiac failure	1 (1.5%)
Chronic obstructive pulmonary disease	3 (4.5%)
Liver disease	4 (6.1%)
Connective tissue disorder	1 (1.5%)
Renal disease	3 (4.5%)
Malignancy	3 (4.5%)
More than $>$ 1 physical illness	14 (21.1%)
Number of participants with at least one physical illness	19 (28.8%)
Number of participants with no physical illness	30 (45.5%)
Severity of COVID illness at time of evaluation	
Asymptomatic	17 (25.8%)
Mild	35 (53.0%)
Moderate	5 (7.6%)
Severe	9 (13.6%)
Reason of admission	
Breathing difficulties/Breathlessness	16 (24.2%)
Fever	18 (27.2%)
Postoperative cases	4 (6.06%)
On chemotherapy	2 (3.03%)
Health care worker (unable to self-isolate)	16 (24.2%)
Oxygen requirement	2 (3.03%)
Others[a]	8 (12.1%)
Oxygen requirement	
Number of patients who required oxygen	26 (39.4%)
Method of oxygen delivery	
Nasal prongs	8 (12.1%)
Venturi mask	18 (27.3%)
Delirium	
History of delirium in the present admission	5 (7.6%)

(*Continued*)

Table 1 (*Continued*)

Variables	Frequency (%)/Mean (SD) ($n = 66$)
Onset of delirium before hospitalization	3 (4.5%)
Onset of delirium hospital emergent	2 (3.0%)

Abbreviations: RT-PCR, reverse transcriptase polymerase chain reaction; SD, standard deviation.
[a]Others - pain abdomen – 2 (3.0%); weakness – 1 (1.5%), posted for surgery – 1 (1.5%), hemoptysis – 1 (1.5%); delivery of baby – 1 (1.5%), chest pain – 1 (1.5%), comorbidities difficult to manage – 1 (1.5%).

Table 2 Cognitive profile of patients with COVID-19 infection as per HMSE and H-MoCA domains ($n = 66$)

Domains of HMSE	Mean (SD); Range/Frequency (%)
Orientation	8.39 (2.28); 1–10; Median – 10.0
Registration	2.92 (0.31); 1–3; Median – 3.0
Attention	4.12 (1.35); 0–5; Median – 5.0
Recall	2.48 (0.89); 0–3; Median – 3.0
Language	8.21 (1.54); 3–9; Median – 9.0
Total HMSE score	26.15 (5.81); 7–30; Median – 30.0
Number of participants	
25–30 points – Normal cognition	47 (71.2%)
21–24 points – Mild dementia	7 (10.6%)
10–20 points – Moderate dementia	11 (16.7%)
$\leq$ 9 points – Severe dementia	1 (1.5%)
No of patients with HMSE score $\leq$24, i.e., cognitive impairment present	19 (28.8%)
Domains of H-MoCA	**Mean (SD); Range/Frequency (%)**
Visuospatial	4.13 (1.47); 0–5; Median – 5.0
Naming	2.66 (0.64); 1–3; Median – 3.0
Attention	5.12 (1.82); 0–6; Median – 6.0
Language	2.13 (0.94); 0–3; Median – 2.0
Abstract	1.54 (0.84); 0–2; Median – 2.0
Delayed recall	3.84 (1.45); 0–5; Median – 4.5
Orientation	4.71 (1.86); 0–6; Median – 6.0
Total MoCA score	24.16 (7.76); 1–30; Median – 28.0
No of patients	
$>$ 26 points – Normal cognition	40 (60.6%)
18–26 points – Mild cognitive impairment	15 (22.7%)
11–17 points – Mild dementia	5 (7.6%)
6–10 points – Moderate dementia	3 (4.5%)
$\leq$ 6 points – Severe dementia	3 (4.5%)
Number of patients with MoCA score $<$ 26, i.e., cognitive impairment present	26 (39.39%)
Number of patients with low cognitive score in MMSE but not in MoCA	2 (3.0%)
Number of patients with low cognitive score in MoCA but not in MMSE	8 (12.1%)
Number of patients with low cognitive score captured by both MMSE and H-MoCA cutoffs	17 (25.8%)

Abbreviations: H-MoCA, Hindi Montreal Cognitive Assessment; HMSE, Hindi Mini-Mental State Examination; MMSE, Mini-Mental State Examination; SD, standard deviation.

Table 3 Anxiety and depression during the hospital stay ($N = 66$)

Variables	Whole sample ($N = 66$) Mean (SD)/Frequency (%)
Mean GAD-7 score	4.84 (4.44); Range: 0–17; Median: 4.0
Severity of anxiety	
Normal (0–4)	36 (54.5%)
Mild (5–9)	17 (25.8%)
Moderate (10–14)	12 (18.2%)
Moderate–Severe (15–19)	1 (1.5%)
Severe ($\geq$ 20)	0
Mean PHQ-9 score	8.96 (4.99), Range: 1–23; Median: 8.5
Severity of depression	
Minimal (0–4)	14 (21.2%)
Mild (5–9)	23 (34.8%)
Moderate (10–14)	19 (28.8%)
Moderately severe (15–19)	8 (12.1%)
Severe ($\geq$ 20)	2 (3.0%)
Overall prevalence	
% of participants having GAD-7 score $\geq$5	30 (45.5%)
% of participants having PHQ-9 score $\geq$10	29 (43.9%)
Number of participants having only anxiety disorder (GAD-7 $\geq$10) but PHQ-9 score of $<$ 10	1 (1.5%)
Number of participants having depression only (PHQ-9 $>$ 10) but GAD-7 score of $<$ 10	18 (27.3%)
Number of participants having both anxiety and depressive disorder (GAD-7 $\geq$10 with PHQ-9 $>$ 10)	11 (16.7%)

Abbreviations:GAD-7, Generalized Anxiety Disorder Questionnaire-7; PHQ-9, Patient Health Questionnaire-9; SD, standard deviation.

Table 4 Relationship of MMSE and MoCA domains with clinical parameters

MMSE domains				
	Age in years *r* (*p*-value)	**Difference between COVID positivity date and ate of evaluation in days *r* (*p*-value)**	**Total PHQ-9 score *r* (*p*-value)**	**Total GAD-7 score *r* (*p*-value)**
Orientation	−0.63 ($<$ 0.001)[a]	0.048 (0.702)	−0.302 (0.014)	−0.232 (0.061)
Registration	−0.242 (0.05)	0.008 (0.947)	0.095 (0.448)	0.144 (0.25)
Attention	−0.642 ($<$ 0.001)[a]	−0.037 (0.768)	−0.368 (0.002)	−0.253 (0.041)
Recall	−0.606 ($<$ 0.001)[a]	−0.108 (0.387)	−0.305 (0.013)	−0.297 (0.015)
Language	−0.413 (0.001)[a]	0.042 (0.736)	−0.304 (0.013)	−0.28 (0.023)
Total MMSE score	−0.615 ($<$ 0.001)[a]	0.005 (0.965)	−0.327 (0.007)	−0.263 (0.033)
H-MoCA domains				
H-MoCA domains	**Age in years *r* (*p*-value)**	**Difference between COVID positivity date and ate of evaluation in days *r* (*p*-value)**	**Total PHQ-9 score *r* (*p*-value)**	**Total GAD-7 score *r* (*p*-value)**
Visuospatial	−0.530 ($<$ 0.001)[a]	−0.062 (0.622)	−0.341 (0.005)	−0.292(0.017)
Naming	−0.433 ($<$ 0.001)[a]	0.01 (0.934)	−0.263 (0.033)	−0.294 (0.017)

(*Continued*)

Table 4 (*Continued*)

MMSE domains				
Attention	−0.489 (< 0.001)[a]	0.054 (0.667)	−0.288 (0.019)	−0.257 (0.037)
Language	−0.526 (< 0.001)[a]	0.012 (0.925)	−0.339 (0.005)	−0.208 (0.094)
Abstract	−0.447 (< 0.001)[a]	−0.17 (0.173)	−0.28 (0.023)	−0.363 (0.003)
Delayed recall	−0.656 (< 0.001)[a]	−0.061 (0.629)	−0.463 (< 0.001)[a]	−0.416 (0.001)
Orientation	−0.633 (< 0.001)[a]	0.015 (0.903)	−0.385 (0.001)[a]	−0.307 (0.012)
Total H-MoCA score	−0.639 (< 0.001)[a]	−0.023 (0.855)	−0.405 (0.001)[a]	−0.357 (0.003)

Abbreviations: GAD-7, Generalized Anxiety Disorder Questionnaire-7; H-MoCA, Hindi Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination; PHQ-9, Patient Health Questionnaire-9.
[a]$p < 0.001$.

Table 5 Comparison of demographic and clinical profile in those with and without cognitive deficits as per MMSE

Variables	Whole sample Frequency (%)/Mean (SD) ($n = 66$)	With normal cognitive profile as per MMSE Frequency (%)/Mean (SD) ($n = 47$)	With low cognitive score as per MMSE < 25 Frequency (%)/Mean (SD) ($n = 19$)	Chi-square/ *t*-test value (*p*-value)
Age	39.85 (16.89) Range: 17–79 Median: 31.5	33.66 (12.70)	55.16 (16.44)	–5.707 (< 0.001)[a]
Age ≥ 65 y	8 (12.1%)	0	8 (100.0%)	–
Gender: Male/Female	40 (60.6%)/26 (39.4%)	26 (55.3%)/ 21 (44.7%)	14 (73.7%)/5 (26.3%)	1.911 (0.167)
Marital status: Married/Single	40 (60.6%)/26 (39.4%)	21 (44.7%)/ 26 (55.3%)	0 /19 (100.0%)	17.34 (< 0.001)[a]
Difference between date of RT-PCR positive and date of cognitive evaluation (in d)	9.34 (4.98); Range: 2–29 Median: 9.0	9.46 (5.65)	10.57 (4.78)	–0.753 (0.454)
Comorbid conditions				
Hypertension	13 (19.7%)	6 (12.8%)	7 (36.8%)	4.95 (0.026)
Diabetes mellitus	13 (19.7%)	5 (10.6%$)	8 (42.1%)	8.47 (0.004)
No of patients with at least one physical illness	19 (28.8%)	12 (25.5%)	7 (36.8%)	0.844 (0.35)
No of patients with no physical illness	30 (45.5%)	27 (57.4%)	3 (15.8%)	FE = 0.003
Severity of COVID illness				
Asymptomatic	17 (25.8%)	14 (29.8%)	3 (15.8%)	1.38 (0.23)
Mild	35 (53.0%)	28 (59.6%)	7 (36.8%)	2.80 (0.09)
Moderate	5 (7.6%)	1 (2.1%)	4 (21.1%)	6.92 (0.008)
Severe	9 (13.6%)	4 (8.5%)	5 (26.3%)	3.64 (0.05)
Oxygen requirement				
Number of participants who required oxygen	26 (39.4%)	10 (21.3%)	16 (84.2%)	22.44 (< 0.001)[a]
Method of oxygen delivery Nasal prongs Venturi mask	8 (12.1%) 18 (27.3%)	4 (8.5%) 6 (12.8%)	4 (21.05%) 12 (63.2%)	1.99 (0.15) 17.32 (< 0.001)[a]

Abbreviations: MMSE, Mini-Mental State Examination; RT-PCR, reverse transcriptase polymerase chain reaction; SD, standard deviation.
[a]$p < 0.001$.

Table 6 Comparison of demographic and clinical profile in those with and without cognitive deficits as per H-MoCA

Variables	Whole sample Frequency (%)/ Mean (SD) ($n = 66$)	With normal cognitive profile as per H-MoCA Frequency (%)/Mean (SD) ($n = 41$)	With low cognitive score as per H-MoCA < 26 Frequency (%)/Mean (SD) ($n = 25$)	Chi-square/ *t*-test value (*p*-value)
Age	39.85 (16.89) Range: 17–79 Median: 31.5	30.44 (9.74)	55.28 (14.65)	−8.27 (< 0.001)[a]
Age ≥ 65 y	8 (12.1%)	0	8 (100.0%)	–
Gender: Male/Female	40 (60.6%)/ 26 (39.4%)	23 (56.1%)/18 (43.9%)	17 (68.0%)/8 (32.0%)	0.922 (0.337)
Marital status Married Single	 40 (60.6%) 26 (39.4%)	 17 (41.5%) 24 (58.5%)	 23 (92.0%) 2 (8.0%)	 16.61 (< 0.001)[a]
Difference between date of RT-PCR positive and date of cognitive evaluation (in d)	9.34 (4.98); Range: 2–29 Median: 9.0	9.75 (5.03)	9.84 (6.08)	−0.061 (0.952)
Comorbid conditions				
Hypertension	13 (19.7%)	4 (9.8%)	9 (36.0)	6.76 (0.009)
Diabetes mellitus	13 (19.7%)	1 (2.4%)	12 (48.0%)	20.38 (< 0.001)[a]
Number of participants with at least one physical illness	19 (28.8%)	9 (22.0%)	10 (40.0%)	2.46 (0.116)
No of patients with no physical illness	30 (45.5%)	27 (65.9%)	3 (12.0%)	FE < 0.001)[a]
Severity of COVID illness at time of evaluation				
Asymptomatic	17 (25.8%)	11 (26.8%)	6 (24.0%)	0.06 (0.79)
Mild	35 (53.0%)	27 (65.9%)	8 (32.0%)	7.84 (0.005)
Moderate	5 (7.6%)	2 (4.9%)	3 (12.0%)	1.02 (0.31)
Severe	9 (13.6%)	1 (2.4%)	8 (32.0%)	10.98 (< 0.001)[a]
Oxygen requirement				
No of participants who required oxygen	26 (39.4%)	6 (14.6%)	20 (80.0%)	27.79 (< 0.001)[a]
Method of oxygen delivery Nasal prongs Venturi mask	 8 (12.1%) 18 (27.3%)	 4 (9.75%) 3 (7.3%)	 4 (16.0%) 15 (60.0%)	 0.56 (0.45) 21.73 (< 0.001)[a]

Abbreviations: H-MoCA, Hindi Montreal Cognitive Assessment; RT-PCR, reverse transcriptase polymerase chain reaction; SD, standard deviation.
[a]$p < 0.001$.

patients had cognitive impairment as per H-MoCA. Overall, about one-fourth of participants had cognitive impairment on both the scales. MoCA has been reported to capture the cognitive deficits in a better way than MMSE and is considered to be more sensitive than MMSE in patients with mild cognitive impairment and poststroke.[26–29] This may explain the higher prevalence of cognitive deficits as per H-MoCA when compared with the HMSE.

A recent study which evaluated cognitive deficits in persons recovered from COVID-19 infection revealed that cognitive deficits were not limited to only those with severe infection but were also seen in those who had mild infection (with no breathing difficulties).[30] Similar findings have been reported by another study from Germany which evaluated 18 young patients during recovery period (median 85 days) and reported mild cognitive deficits in three-fourths (78%) of the participants based on the Modified Telephone Interview for Cognitive Status scale.[31] Studies which have evaluated persons who have recovered from COVID-19 infection, have also documented significant cognitive deficits (~80%) in persons who had hypoxia or required intubation during their hospital stay.[11] As compared with these studies, the prevalence of cognitive impairment in our study sample is quite low, which could be due to restriction of study participation to those who were clinically stable, but still were in the acute phase of the infection. Irrespective of this fact, presence of cognitive deficit in about one-fourth of the participants, especially those who had mild infection and did not require oxygen support suggest that the COVID-19 virus infects the neurons and can have significant impact on cognitive functioning. This finding suggests that the COVID-19 infection may possibly leave a scar on human brain and we

may see increase in the prevalence of dementia and mild cognitive impairment in times to come.

The studies which had evaluated cognitive deficits in persons who have recovered from COVID-19 infection suggest deficits predominantly in the area of working memory,[11,32] attention, processing speed and reaction time,[11,12] executive functioning, and visuospatial functions (as per MoCA).[33] The present study also confirms similar deficits, suggesting that all neurocognitive domains are affected during the acute phase of illness.

Anxiety and depressive symptoms have been reported in hospitalized patients with COVID-19.[34,35] The present study findings found depressive symptoms in more than two-fifths of the patients (43.9%) and anxiety symptoms in approximately 45% of study sample, with approximately 16.7% of participants screening positive for both anxiety and depression. These prevalence rates are similar to the previous studies.[36,37]

A study which had evaluated cognitive deficits in the postcritical acute stage of severe COVID-19 infection, reported that mental fatigue and depressive and anxiety symptoms to be associated with cognitive slowness and all these correlate with the MoCA score.[33] This suggests that anxiety and depressive symptoms can affect the cognitive functions. In the present study too, a higher depressive (total PHQ-9 score) and a higher anxiety score (total GAD-7 score) correlated with higher level of cognitive impairment in almost all the domains of cognition. However, when controlled for multiple comparisons, these became insignificant and hence a larger sample size would give more clear inferences.

The study also revealed that those with low cognitive scores during the acute phase of illness were more among those who were of older age, had diabetes mellitus, moderate COVID-19 infection, and require oxygen support during their hospital stay. These findings are in line with the existing literature (on recovered patients) that have documented higher level of cognitive deficits in the elderly, those with multiple comorbidities, and in those who required intubation/oxygen support during acute phase of infection.[11,12,33]

Our study has few limitations which include cross-sectional assessment, small sample size, relatively more number of patients with mild or asymptomatic COVID-19 infection, and assessment of limited number of neurocognitive domains. As this was an exploratory study, we did not evaluate the relationship of cognitive functioning with biochemical and laboratory findings (such as interleukins levels, D-dimer levels, CT score, CRP levels, etc.). Further, we had assessed the patient when they were ill and hospitalized (though clinically stable to participate). These factors can affect the evaluation. The absence of a control group (hospitalized patients with any other illness) for comparison can also be considered as another limitation of our study. Further, we have not taken into account the confounding effect of diabetes mellitus, age, and other comorbid conditions on cognitive functioning. Hence, the findings should be interpreted keeping these limitations in mind. However, the strengths of the study include assessment of stable patients during their acute phase of illness and sample size being more than some of the earlier studies,[11,12,33] which were mostly conducted in recovered patients.

To conclude, the present study reveals that low cognitive scores are seen in about one-fourth of the persons with acute COVID-19 infection, which are more prevalent among the elderly, those with diabetes mellitus, and those who required oxygen support prior to the assessment. As more and more literature is emerging on the presence of neurological and psychiatric sequelae (intracranial hemorrhage, ischemic stroke, parkinsonism, dementia, anxiety disorder, and psychotic disorder) in persons who have recovered from COVID-19 infection, there is a need for more extensive neurocognitive evaluation for these patients and to start cognitive rehabilitation at the earliest.

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Conflict of Interest
None declared.

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