**NOT PEER-REVIEWED**

# Cognitive Assessment in Asymptomatic COVID-19 Subjects

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## ABSTRACT

**Background**

Neurological features of COVID-19 have been reported in addition to the respiratory manifestations, but cognitive dysfunction has been scarcely described. And cognitive assessment has not been studied in asymptomatic subjects.

**Method**

We compared the cognitive assessment scores between asymptomatic SARS-CoV-2 infected subjects with that of controls to detect mild cognitive impairment by the Montreal Cognitive Assessment test.

**Result**

Asymptomatic COVID-19 subjects secured lower scores in certain domains of the MoCA in comparison with the controls. The domains were visuoperception ($2.4\pm0.7$ vs$2.8\pm0.7$, p=0.032), naming ($3.6\pm0.5$ vs$3.9\pm0.2$, p=0.016) and fluency ($0.9\pm0.6$ vs$1.6\pm0.7$, p=<0.001). Also, older aged COVID-19 positive subjects scored lower in the MoCA when compared to the younger people.

**Conclusion**

Our study shows that even otherwise asymptomatic COVID-19 subjects have cognitive deficits in certain subdomains and suggests the need for a detailed psychometric assessment especially in the elderly population.

**Keywords:** COVID-19 neurological; COVID-19 psychiatric; COVID-19 cognition

## 1 Introduction

COVID-19, caused by SARS-CoV-2 has killed millions of people across the world in less than a year. It has affected almost all of the human population directly or indirectly. Directly by causing a spectrum of disorders ranging from no symptoms to death. Indirectly by resulting in sickness or loss of a family member or socioeconomic turbulence due to restricted movement of parcels and people [1]. The people afflicted with SARS-CoV-2 were reported to have respiratory symptoms in the earliest studies. Thereafter a number of extra respiratory features were also observed. These included neurological deficits also. Some of these

were stroke, seizures, neuropathy and movement disorders [2]. Recent pathological studies have shown the neurotropism of SARS-CoV-2, thus establishing a direct pathophysiological basis to the neurological features [3].

Neurological features of higher mental functions were reported by Zhou et al who performed a study on the cognitive functions of 29 COVID-19 recovered patients. The patients secured lower scores in Continuous Performance Test (which is used to assess attention and impulse) than the controls [4]. Others have reported a dysexecutive syndrome in the COVID-19 patients [5]. Thus, symptomatic patients do suffer cognitive deficits in addition to the earlier reported neurological features. Neurological features such as weakness, pain and numbness are reported readily as they are easily noticed by the patients. However, dysfunctions of the higher mentation go unnoticed especially if they are mild and occur in otherwise asymptomatic persons [6]. Such unrecognised deficits have been brought out in asymptomatic subjects in many other diseases by targeted cognitive tests like MiniMental Status Examination (MMSE) and Montreal Cognitive Assessment (MoCA) [7,8]. Although MMSE has been widely used for detecting cognitive impairment, it has been found inferior [9] to the MoCA in detecting Mild cognitive impairment (MCI). MoCA has been widely validated in diagnosing MCI in many studies [6]. We used the MoCA test to detect MCI in asymptomatic COVID-19 subjects.

## 2 Methods

As a case control study at the department of General Medicine, Great Eastern medical School and Hospital, Ragole, India we compared the cognitive assessment scores of 93 asymptomatic COVID-19 subjects with those of 102 controls. The study was conducted from June 2020 to July 2020. Laboratory-confirmation of SARS-CoV-2 infection was done by RT-PCR on nasopharyngeal swabs. The subjects were recruited from relatives of COVID-19 patients brought to the hospital. Control subjects were negative for the infection. All subjects with age <18 years, comorbidities, psychiatric illness or if on any medication were excluded. The sample size was calculated to 91 cases and 91 controls based on the previous study by Zhou *et al.* We recruited 105 subjects in each group. The subjects were then administered the MoCA basic test in the local language as all of them had less than four years of education. MoCA includes nine domains: executive function, fluency, orientation, calculation, abstraction, delayed recall, visuoperception, naming and attention. Cognitive impairment is defined as score less than or equal to 26 out of 30. The scores were compared between cases and controls. Permission was obtained to use the MoCA for the study. The data was analyzed using IBM SPSS Statistics-version 21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.). The data is presented as mean and standard deviation. Tests of significance used were t-test, one-way ANOVA for parametric data. The data is available with the corresponding author.

## 3 Results

In our study we finalised 93 asymptomatic COVID-19 patients and 102 controls after exclusion due to lack of consent and insufficient data. The mean age of the patients was 36.2±11.7 and that of the controls was 35.6±9.8. In the COVID-19 subjects 52.3% were women and in the controls 54.7% were women.

There was no significant difference in the overall cognitive assessment scores between the two groups, but COVID-19 patients secured lower scores than controls in the domains of visuoperception, naming and fluency. (Table 1)

Also, COVID-19 positive subjects aged greater than 50 years scored lower in the MoCA when compared to the younger people. (Table 2). There were no differences between the two genders (Supplementary table).

**Table 1:** *Montreal Cognitive Assessment scores of the subjects*

| Domain (Max. score) | Asymptomatic COVID-19 subjects (93) | Controls (102) | p value | 95%CI |
|---|---|---|---|---|
| Mean Total Score (30) | 26±2.6 | 26.1±3.0 | 0.887 | -1.492 to 1.292 |
| Executive function (1) | 0.9±0.2 | 0.9±0.2 | 1 | -0.105 to 0.105 |
| Fluency (2) | 0.9±0.6 | 1.6±0.7 | *<0.001* | -1.002 to -0.378 |
| Orientation (6) | 5.6±0.6 | 5.6±1 | 1 | -0.353 to 0.353 |
| Calculation (3) | 2.4±0.8 | 2.4±0.9 | 1 | -0.426 to 0.426 |
| Abstraction (3) | 2.8±0.5 | 2.6±1 | 0.209 | -0.114 to 0.514 |
| Delayed recall (5) | 3.1±1.1 | 3.2±1 | 0.728 | -0.668 to 0.468 |
| Visuoperception (3) | 2.4±0.7 | 2.8±0.7 | *0.032* | -0.766 to -0.034 |
| Naming (4) | 3.6±0.5 | 3.9±0.2 | *0.016* | -0.545 to -0.055 |
| Attention (3) | 2.5±0.5 | 2.6±0.8 | 0.496 | -0.390 to 0.190 |

**Table 2:** *Age wise comparison of the MoCA scores.*

| | Age 18 - 29 | 30 - 49 | 50 and above | P value |
|---|---|---|---|---|
| Mean MoCA Score in Cases | 25.9±2.1 | 25.9±2.3 | 24±3.5 | *0.018* |
| Mean MoCA Score in Controls | 27±1.7 | 25.6±4.3 | 24.5±3.5 | 0.537 |

Number of Cases =33 (Age 18 – 29) vs 42 (30-49) vs 18 (50 and above). Number of Controls 48 vs 42 vs 12.

**Cases**

Tukey HSD Post-hoc Test...

Age 18 - 29 vs Age 30 - 49: Diff=0.0000, 95%CI=-1.3905 to 1.3905, p=NaN

Age 18 - 29 vs Age 50 and above: Diff=-1.9000, 95%CI=-3.6515 to -0.1485, p=0.0302

Age 30 - 49 vs 50: Diff=-1.9000, 95%CI=-3.5840 to -0.2160, p=0.0230

**Controls**

Tukey HSD Post-hoc Test...

Age 18 - 29 vs Age 30 - 49: Diff=-1.4000, 95%CI=-5.7355 to 2.9355, p=0.6821

Age 18 - 29 vs Age 50 and above: Diff=-2.5000, 95%CI=-9.1226 to 4.1226, p=0.5961

Age 30 - 49 vs Age 50 and above: Diff=-1.1000, 95%CI=-7.8166 to 5.6166, p=0.9044

## 4    Discussion

We found that asymptomatic COVID-19 patients had impairments in certain cognitive domains. They included visuoperception, naming and fluency. Older patients had more MCI compared to the subjects below 50 years of age. Our study adds to the Zhou et al study that showed defects of CPT in COVID-19 patients and extends the neurological spectrum even to otherwise asymptomatic subjects. These findings confirm the cognitive impairments due to COVID-19.

The dysfunction in multiple cognitive domains corresponds to dysfunction of multiple parts of the brain [10]. This is in line with previous neuropathological [11,12] and neuroimaging studies [13] which have shown that viral pathology involves most of the brain. These neurological patterns have been associated with most of the corona viruses [14]. Direct neural invasion, neuroinflammation and systemic proinflammatory state and hypoxia have all been suggested to mediate the neurological dysfunction in COVID-19 [15]. An interesting study has shown that asymptomatic subjects also may have pneumonia discernible only by imaging [16]. It may even be possible that the MCI in our COVID-19 subjects might be due to impaired oxygen supply to the brain [15], keeping in mind that even hypoxia goes undetected in some patients even with a pulse oximeter [17].

Our finding of cognitive impairment in asymptomatic COVID-19 patients is important especially in elderly patients if they already have MCI. It might be further compromised. Even without other symptoms they might thus need more vigilant care [18] as their activities of daily living [ADL] might be affected.

From our findings, it may be suggested that people employed in highly intellectual occupations might fall short of their work requirements if they have COVID-19 infection even asymptomatically. This is pertinent as doctors and medical personnel who are at a very high risk for the infection come under this category and their mental health condition is paramount to every medical strategy against COVID-19.

Previous literature has hypothesized that COVID-19 affected patients might be at high risk of developing cognitive decline after overcoming the primary infection [19]. The cognitive impairment reported in our study and the previous studies [4,5] suggests the need for long term follow up of the COVID-19 affected subjects as people with MCI are prone to dementia [20].

## 5    Conclusion

Our study shows that even otherwise asymptomatic COVID-19 subjects have cognitive deficits in certain subdomains and suggests the need for a detailed psychometric assessment especially in the elderly population.

## 6    Declarations

### 6.1    Study Limitations

Our study is limited by the small sample and the hospital bias but it suggests MCI in asymptomatic COVID-19 subjects. And since only one test was done, a full psychometric assessment study is warranted to fully understand the pattern better.

### 6.2    Authorship contributions

Conceptualization SA
Methodology SA and KVRA
Formal Analysis SA, KVRA and JJP
Investigation SA, KVRA and JJP
Original Draft Preparation SA
Review & Editing SA, KVRA and JJP

### 6.3 Acknowledgements

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### 6.4 Competing Interests

The Authors declare that there is no conflict of interest

### 6.5 Ethical Approval

The Institutional Ethical Committee at GEMS, Ragole approved the study. (12/IEC/GEMS&H/2020).

### 6.6 Informed Consent

Written informed consent was taken from the subjects.

## 7 Supplementary Table

Gender wise MoCA score comparison

Cases 49m vs 51f.  Controls 44m vs 56f

|  | Males | Females | P value | 95%CI |
|---|---|---|---|---|
| Mean MoCA Score in Cases | 25.4±2.7 | 25.8±2.5 | 0.49 | -0.762 to 1.562 |
| Mean MoCA Score in Controls | 27.2±2.6 | 25.5±3.4 | 0.31 | -5.114 to 1.714 |

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