COGNITIVE FUNCTIONS AMONG PATIENTS WHO RECOVERED FROM COVID-19

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Abstract

Introduction: The Coronavirus disease 2019 (COVID-19) spread, causing a worldwide pandemic and affecting multiple organs and systems. The possible long-term sequelae of COVID-19 have become an increasing concern. Currently, little information exists about prolonged COVID-19 affects related to cognitive functions.

Objective: The study aimed to investigate the cognitive functions of patients who recovered from COVID-19 at least three months after the diagnosis.

Methods: A cross-sectional study was conducted to investigate cognitive functions among 150 employees of Buddhasothorn Hospital, Chachoengsao, Thailand. Of these, 75 employees had a history of COVID-19 at least three months after the diagnosis. Demographic characteristics were recorded and screened for depression, anxiety and insomnia. They were tested for their cognitive functions using the Montreal Cognitive Assessment (MoCA) and compared with 75 employees without a history of COVID-19.

Results: All postCOVID-19 cases presented mild COVID-19 symptoms. The results showed that 96% of COVID-19 in both groups, cases and the healthy group, had normal cognitive functions using the MoCA that did not significantly differ. However, the depression score in the postCOVID-19 cases was significantly higher than that of the participants without a history of COVID-19 (1.09 ± 1.36 and 0.61 ± 1.09, respectively (p = 0.018). Regression analysis between the postCOVID-19 cases and depression using multivariate analysis showed that the postCOVID-19 cases were associated with depression scale (β coefficient=0.470; 95%CI: 0.073, 0.867, respectively), after adjusting for age, sex, educational level and underlying diseases.

Conclusion: The cognitive functions of employees having a history of COVID-19 and without infection did not differ.

Keywords: Postacute COVID-19, Cognitive impairment, MoCA

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Introduction

In late 2019, the Coronavirus Disease 2019 (COVID-19) began to spread, causing a worldwide pandemic. Then March 11, 2020, the World Health Organization (WHO) announced that COVID-19 was a global public health problem.[1] COVID-19 could affect multiple organs and systems. Moreover, people who survived COVID-19 complained of a variety of symptoms. The most common symptoms reported were fatigue, headache, attention disorder, hair loss and dyspnea.[2-4] Consequently, the possible long term sequelae of COVID-19 have become an increasing concern. Likewise, to date, more information is needed about the long term sequelae of COVID-19. These studies also reported prolonged COVID-19-related cognitive impairment [5, 6] and unrelated cognitive functions.[7] We are interested in employees of the Buddhasothorn Hospital, Chachoengsao, because they gained a good education regarding COVID-19. Therefore, the present study aimed to investigate the cognitive functions of patients who had recovered from a COVID-19 at least three months after the diagnosis. The secondary objective was to study depression, anxiety and insomnia associated with COVID-19.

Methods

The study was approved and followed the Ethics principles of the Buddhasothorn Hospital (BSH-IRB number 015/2565). Between 1 September and 15 October 2022, a cross-sectional study was conducted among employees of a tertiary care hospital, the Buddhasothorn Hospital, Chachoengsao Province, Thailand. The participants were chosen using a purposive sampling technique from employees of the Buddhasothorn Hospital. Written informed consent was obtained from enrolled participants. We enrolled 75 employees who had recovered from COVID-19. All were confirmed positive for COVID-19 results using either a real-time polymerase chain reaction (RT-PCR) test or an antigen test kit (ATK) for COVID-19; participants were diagnosed at least three months beforehand. Next, 75 employees without a history of COVID-19 were enrolled. All participants were 18 to 60 years old, had not taken the Montreal Cognitive Assessment (MoCA) before and were free of depression, anxiety and insomnia.

The participants were interviewed for general personal information (sex, age, education and underlying diseases) and information about their COVID-19 illness (detection of the infection, severity of the symptoms and length of time of the symptoms). They were screened for depression and anxiety using the Thai Hospital Anxiety and Depression Scale (THAI HADS), [8] screened for insomnia using the Epworth Sleepiness Scale (ESS) [9] and tested for their cognitive functions using the MoCA.[10]

Assessment Tools

The MoCA Thai Version [10] is considered a measure for general cognitive impairment (visuospatial and executive functions, naming, attention, calculation, language, verbal abstraction, delay recall and orientation) assessed by a researcher trained in the evaluation of the test. The maximum MoCA score was 30 points (an additional point was given to a person with ≤12 years of education). The cut-off score for defining cognitive impairment was <25. The THAI HADS [8] was used to measure anxiety and depression, and the cut-off score was ≥11. The ESS [9] was used to measure, and the cut-off score was >10.

Statistics analysis

The baseline demographic and clinical characteristics of postCOVID-19 and healthy subjects were presented as frequencies or percentages and compared using the Chi-square or Fisher's exact tests, as appropriate. Continuous variables were presented as the means ± standard deviation (SD) (in the case of normal distribution), medians, and interquartile range, as appropriate. These were compared using the independent samples t-test and Mann-Whitney U test to correlate the mean score of the cognitive functions, anxiety, depression and daytime sleepiness.

To analyze the relationships among the dependent and independent variables including factors, cognitive functions, depression, anxiety

and insomnia, univariate and multivariate linear regression analyses were used. A two-sided α level of 0.05 was used for all tests.

Results

The demographic and clinical characteristics of the participants with and without a history of COVID-19 are shown in **Table 1**. The mean age, sex, level of education and underlying diseases did not significantly differ. They reported the following symptoms during the acute phase of the infection: cough (46.7%), anosmia (25.3%), fatigue (21.3%), dyspnea (17.3%), cognitive complaint (9.3%) and myalgia (8%). Additionally, the median duration of postCOVID-19 was two-weeks (IQR: 2 to 4).

Table 1. Demographics and clinical characteristics of participants with a history of COVID-19 and those without

Characteristic	Participants with a history of COVID-19 (n = 75)	Participants without a history of COVID-19 (n = 75)	*p*-value
Age (years)	36.28 ± 10.49	36.97 ± 12.59	0.715[t]
Sex			
Female	65 (86.7)	66 (88.0)	0.806[c]
Male	10 (13.3)	9 (12.0)	
Education			
Primary school	0 (0.0)	2 (2.7)	0.279[f]
Secondary school	9 (12.0)	5 (6.7)	
Bachelor's degree or higher	66 (88.0)	68 (90.7)	
Underlying disease			
Yes	20 (26.7)	17 (22.7)	0.570[c]
No	55 (73.3)	58 (77.3)	
AR			
Yes	6 (8.0)	5 (6.7)	0.754[c]
No	69 (92.0)	70 (93.3)	
DM			
Yes	3 (4.0)	4 (5.3)	1.000[f]
No	72 (96.0)	71 (94.7)	
HT			
Yes	2 (2.7)	3 (4.0)	1.000[f]
No	73 (97.3)	72 (96.0)	
DLP			
Yes	1 (1.3)	1 (1.3)	1.000[f]
No	74 (98.7)	74 (98.7)	
Thyroid			
Yes	3 (4.0)	0 (0.0)	0.245[f]
No	72 (96.0)	75 (100.0)	
Others			
Yes	7 (9.3)	4 (5.3)	0.347[c]
No	68 (90.7)	71 (94.7)	

Table 1. Demographics and clinical characteristics of participants with a history of COVID-19 and those without (Cont.)

Characteristic	Participants with a history of COVID-19 (n = 75)	Participants without a history of COVID-19 (n = 75)	*p*-value
Covid-19 symptoms			
Anosmia	19 (25.3)		
Fatigue	16 (21.3)		
Dyspnea	13 (17.3)		
Cough	35 (46.7)		
Cognitive impairment	7 (9.3)		
Myalgia	6 (8.0)		
Other symptoms postCovid	3 (4.0)		
Duration of symptoms (weeks)	2 (2 - 4)		
Oxygenation	0 (0.0)		

Data were presented as a number (%), mean ± standard deviation or median (interquartile range). The *p*-value corresponded to the independent samples t-test, [m]Mann-Whitney U test, [c]Chi-square test, or Fisher's exact test.

The MoCA results of cognitive impairment among participants with and without a history of COVID-19 were equal to 4% each. The language score was significantly higher among participants with a history of COVID-19 than among those without a history (2.73 ± 0.53 postCOVID-19 patients; 2.48 ± 0.74 healthy controls; $p = 0.017$). Other scores did not significantly differ between the groups; the mean MoCA score was 27.75 ± 1.69 among participants with a history of COVID-19 and 27.36 ± 1.62 among those without ($p = 0.154$) (**Table 2**).

The mean anxiety scores of the THAI HADS among participants with a history of COVID-19 and those without were 2.04 ± 1.79 and 1.92 ± 1.73, respectively ($p = 0.677$). The mean score for doubtful cases (8 to 10) was 0.0% and 1.3%, respectively ($p = 1.000$). On the other hand, the mean depression score of the THAI HADS was significantly higher among participants with a history of COVID-19 compared with those without a history (1.09 ± 1.36 and 0.61 ± 1.09, respectively ($p = 0.018$)). (**Table 2**)

The mean scores of the ESS among participants with a history of COVID-19 and those without did not significantly differ for daytime sleepiness (3.17 ± 2.55 and 2.64 ± 2.74, respectively ($p = 0.219$)). The ESS scores among participants with and without a history of COVID-19 were 2.7 and 5.3%, respectively (**Table 2**).

Analysis of the relationship between post COVID-19 status and cognitive impairment, depression, anxiety and daytime sleepiness is shown in **Table 3.** The results of the regression analysis between postCOVID-19 status and cognitive impairment using univariate analysis and multivariate analysis showed that post-COVID-19 status had a statistically insignificant MOCA score (β coefficient = 0.387; 95% CI= -0.146, 0.919 and β coefficient = 0.381; 95%CI= -0.107, 0.868, respectively) after adjusting for age, sex, educational level and underlying diseases.

Regression analysis between the post-COVID-19 status and anxiety using univariate and multivariate analysis showed that post-COVID-19 status had no significant anxiety scale (β coefficient=0.120; 95% CI =-0.448, 0.688 and β coefficient=0.108; 95%CI: -0.455, 0.671, respectively), after adjusting for age, sex, educational level and underlying diseases.

Table 2. Comparison of the cognitive functions, anxiety, depression and daytime sleepiness between participants with a history of COVID-19 and those without

Characteristic	Participants with a history of COVID-19 (n = 75)	Participants without a history of COVID-19 (n = 75)	*p*-value
Montreal Cognitive Assessment (MoCA)			
Visuospatial/executive	4.85 ± 0.36	4.87 ± 0.34	0.815[t]
Naming	2.99 ± 0.12	2.97 ± 0.16	0.563[t]
Memory	1.00 ± 0.00	1.00 ± 0.00	NA
Attention	5.89 ± 0.35	5.89 ± 0.31	1.000[t]
Language	2.73 ± 0.53	2.48 ± 0.74	0.017[t]
Abstraction	1.95 ± 0.28	1.96 ± 0.26	0.761[t]
Delayed recall	3.36 ± 1.32	3.16 ± 1.27	0.347[t]
Memory index Score (MIS)	12.32 ± 2.34	11.68 ± 2.49	0.107[t]
Orientation	5.97 ± 0.16	6.00 ± 0.00	0.159[t]
MOCA score	27.75 ± 1.69	27.36 ± 1.62	0.154[t]
Cognitive impairment	3 (4.0)	3 (4.0)	1.000[f]
Anxiety	2.04 ± 1.79	1.92 ± 1.73	0.677[t]
Noncases (0-7)	75 (100)	74 (98.7)	1.000[f]
Doubtful cases (8-10)	0 (0.0)	1 (1.3)	
Depression	1.09 ± 1.36	0.61 ± 1.09	0.018[t]
Noncases (0-7)	75 (100)	75 (100)	NA
Epworth Sleepiness Scale	3.17 ± 2.55	2.64 ± 2.74	0.219[t]
Excessive daytime sleepiness (ESS score ≥10)	2 (2.7)	4 (5.3)	0.681[f]

The data were presented as a number (%), mean ± standard deviation or median (interquartile range). The P-value corresponded to the independent samples t-test, [m]Mann-Whitney U test, [c]Chi-square test, or Fisher's exact test.

Table 3 Multiple linear regression analysis for the association between COVID-19 with cognitive function, anxiety, depression and sleepiness

Outcome	B	(95%CI)	SE(B)	*p*-value
Univariate analysis				
MoCA Score	0.387	(-0.146, 0.919)	0.270	0.154
Anxiety subscale	0.120	(-0.448, 0.688)	0.287	0.677
Depression subscale	0.480	(0.083, 0.877)	0.201	0.018*
Epworth Sleepiness Scale	0.533	(-0.321, 1.388)	0.432	0.219
Multivariate analysis				
MoCA Score	0.381	(-0.107, 0.868)	0.247	0.125
Anxiety subscale	0.108	(-0.455, 0.671)	0.285	0.706
Depression subscale		(0.073, 0.867)	0.201	0.021*
Epworth Sleepiness Scale		(-0.321, 1.383)	0.431	0.220

Abbreviations: MoCA: Montreal Cognitive Assessment, B: β coefficient, SE(B): Standard error of B,
[a]Multiple linear regression model adjusted for age, sex, education and underlying disease
* Significant at $p < 0.05$

Regression analysis between postCOVID-19 status and daytime sleepiness using univariate and multivariate analysis showed that the post-COVID-19 status had a statistically insignificant Epworth sleepiness scale score (β coefficient= 0.533; 95%CI: -0.321, 1.388 and β coefficient = 0.531; 95%CI: -0.321, 1383, respectively), after adjusting for age, sex, educational level and underlying diseases.

On the other hand, regression analysis between postCOVID-19 status and depression using univariate and multivariate analysis showed that postCOVID-19 status was associated with depression scale (β coefficient = 0.480; 95% CI: 0.083, 0.877 and β coefficient = 0.470; 95% CI: 0.073, 0.867, respectively), after adjusting for age, sex, educational level and underlying diseases.

Discussion

This study showed that patients, who had recovered from a COVID-19 for at least three months, had the most common postCOVID-19 symptoms of cough, anosmia, fatigue, dyspnea, cognitive complaint and myalgia, which was similar to related studies.[2, 3] Furthermore, they had symptoms for about two weeks, similar to an earlier study by Tenforde et al.[11] Our studies were conducted on young patients with a mild COVID-19. They did not need oxygen therapy during the course of the infection; thus, leading to a quicker recovery. These symptoms were similar to postviral syndromes, such as influenza, Epstein-Barr virus and herpes.

The present study was conducted in a selected population of participants working in the Buddhasothorn Hospital. Therefore, the characteristics of the postCOVID-19 and healthy subjects did not differ regarding age, sex, educational level and underlying diseases. Both groups also had MoCA scores that did not significantly differ. [12-15] This result differed from related studies, possibly due to the population (age, degree of COVID-19, level of education and underlying diseases), neuropsychological assessment and design study. These related studies presented that postCOVID-19 status impaired cognitive functions such as executive function, attention, short term memory, language tasks and visuospatial processes. On the other hand, this study was similar to the related study of Mattioli et al.[7]Those participating in the study experienced a mild degree of COVID-19, obtained a high level of education and presented fewer comorbidities. This study showed that the language score in the postCOVID-19 group was higher than that of the healthy control, possibly due to excitement during the test. Some participants could follow the sentences correctly when consciously repeated, and they tended to lose points on the first test's sentence. Although the participants did not experience anxiety, depression or daytime sleepiness, the depression score of the THAI HADS in the post COVID-19 group was higher than that of the healthy control. This was similar to the related studies of Del Rio et al. [6] Mattioli et al. [7] and Woo et al.[14] reporting that patients who had recovered from COVID-19 experienced depression. Moreover, the results correlated between depression and MOCA score, which was known to affect cognitive impairment.

The main limitations of this research were a small sample size of studied subjects and mainly young patients with mild COVID-19 symptoms with a high education level. Therefore, analysis of large cohorts of patients with postCOVID-19 status could not be conducted. In addition, some risk factors of cognitive decline were not identified. However, to our knowledge, this constitutes one of the earliest studies in Thailand to investigate cognitive functions among patients who recovered from COVID-19. Further studies should be examine more neuropsychological and neuroimaging changes, which might yield more reliable results.

Conclusion

The results of this study demonstrated that cognitive functions amng young patients who had recovered from COVID-19 for at least three months after the diagnosis with mild COVID-19 symptoms did nodiffer from those without a history of COVID-19.

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