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Survey of Cognitive function in hospitalized patients recovering from COVID-19

Ghoreishi F.S.[1] *MD*, Nourian R.[1]* *MD*, Shafaei M.Sh.[2] *MD*, Assarian F.[1] *MD*

[1] Psychiatric Department, Medicine Faculty, Kashan University of Medical Sciences, Kashan, Iran
[2] Medical Student Department, Medicine Faculty, Kashan University of Medical Sciences, Kashan, Iran

Abstract

Aims: COVID- 19 is a highly prevalent infectious disease with several systemic complications, including neurological and psychological complications.This study aimed to evaluate the status of cognitive function of individuals improved by COVID- 19 in 2021.

Instrument & Methods: The present cross-sectional study was performed on 309 patients recovered from COVID- 19.Cognitive function assessment was performed using the Addenbrooke Cognitive Test (ACE-R).

Findings: In this study, 309 patients recovered from COVID-19 with a mean age of 44.90 9 9.45 years (range 21-59) participated. The mean cognitive function of participants was 88.86 7 7.26 which have achieved nearly 89% of the total score (100 points) and indicates the normal cognitive function of individuals. There was a significant relationship between cognitive function (and all its components) in individuals with the variables of age, education, and employment. In addition, the rate of cognitive function (and all its components except expressive language) in people with intubation were significantly less than those who had not been intubated during treatment. A total of 18 patients (5.8%) had an abnormal cognitive function.

Conclusion: The findings showed that cognitive impairments there are even in patients recovering from COVID-19 and may be associated with underlying inflammatory processes.

Keywords

Cognitive Function [Not in MeSH];
Hospitalization [https://www.ncbi.nlm.nih.gov/mesh/68006760];
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*Corresponding Author
Tel: +98 (31) 55549111
Fax:-
Post Address: Kashan University of Medical Sciences, Kashan, Iran. Postal Code: 8715973446
psychiatric.department@gmail.com
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Introduction

Coronavirus 2019 is a respiratory syndrome caused by the RNA virus [1].This disease can lead to several complex syndromes due to its wide and variable effects on the human body. In many viral infections, immune cells detect pathogenesis and activate the inflammatory response, which triggers a wide range of effects, including the spread of pathogens, or the molecular signals that regulate inflammation. This reciprocal expansion causes a cytokine storm or an increase in the instability of inflammatory cytokines in the bloodstream [2].

Almost a year after the first outbreak of COVID-19, we still do not know much about how the virus works and how it affects health. However, many patients recovering from COVID-19 have been found to have neurological, psychiatric, and cognitive problems[3-6].These symptoms are estimated to be present in up to one-third of COVID-19 patients admitted to the hospital [5, 6].These symptoms appear to persist long after recovery from the initial infection and have detrimental effects on the patient's quality of life[5, 7-9].Past respiratory viral pandemic studies suggest that a variety of neuropsychiatric symptoms can occur in the context of an acute viral infection or after several periods following infection. Reports from the 18th and 19th centuries indicate that influenza pandemics have been associated with an increased incidence of various neuropsychiatric symptoms, such as insomnia, anxiety, depression, mania, psychosis, suicidal ideation, and delirium. Encephalitis lethargica (EL), for example, is an inflammatory disorder of the central nervous system characterized by hyper somnolence, psychosis, catatonia, and Parkinsonism that increased around the time of the Spanish flu pandemic in the early 20th century. Evidence of acute neuropsychiatric symptoms is emerging in the acute cases of COVID 19. In an initial report of 217 patients admitted to Wuhan, China, neurological manifestations were seen in approximately half of the patients with severe infections (40 of 88), including brain complications, Vascular (such as stroke) encephalopathies, and muscle injuries [10].

Cognitive deficits occur frequently following critical illness and are usually resistant and debilitating [11, 12]. They are known as a common complication of COVID-19.Several factors associated with the disease and its treatment may contribute to cognitive impairment. These include hypoxia, mechanical ventilation, sedation, delirium, cerebrovascular events, and inflammation [6, 13-15]. In a study of patients with MERS, three patients with severe neurological syndrome presented with altered levels of consciousness ranging from confusion to coma, ataxia, and focal motor impairment. MRI of the brain showed significant changes with extensive bilateral hypertensive lesions (on T2 imaging) in white matter and subcortical areas of the frontal, temporal and parietal lobes, basal ganglia, and callus of the body [14]. Zhou's study in 2020 showed that cognitive impairment there is in recovered patients from COVID-19 [16]. In 2021, Jaywant reports that 81% of patients after recovering from coronavirus disease had cognitive dysfunction [17].

Due to the pandemic of COVID-19, as well as the variable complications and the resulting multiple organ failures, we decided to investigate neuropsychological complications such as cognitive disorders in patients improved from COVID- 19 in Kashan Hospital of Shahid Beheshti in 2021.

Instrument and Methods

This is a cross-sectional study that was performed on 362 patients recovering from COVID-19 disease. The study population was patients recovering from COVID- 19 disease who had a record of hospitalization in Kashan Hospital of Shahid Beheshti in 2021.The sampling method was as follows: first, permission was obtained from the head of the hospital to access the information of patients that discharged from COVID-19 disease, then by referring to the hospital archives, a list of all patients was prepared and a code was given to each patient, with Considering the principle of confidentiality, the samples were selected using a random number table. In the next step, patients were contacted and invited to complete the questionnaire. Written consent was obtained from the samples before completing the questionnaire.

Inclusion criteria in this study were included; people who had been discharged and improved from COVID-19 and one month had passed since their discharge, the patients aged 20 to 60 years, the patients who had at least a basic literacy. Exclusion criteria included the patients who scored less than 11 on the HADS (Hospital Anxiety and Depression Scale) questionnaire, the patients who reported a history of anxiety disorders and depression and psychiatric illness, as well as history of hospitalization and psychiatric medication use.

The Eden brook Cognitive Test is a developed format of the Mini-Mental State Examination (MMSE), which includes five cognitive domains: attention/orientation, memory, language, verbal fluency, and visual-spatial skills. This test has high sensitivity and specificity [18]. This questionnaire includes the following components:

Attention; is tested by asking the patient about the date, including the current season and location. The patient repeats three simple words and subtracts the serial.

Memory; by asking the patient to recall three words that have already been repeated, to remember and recall an imaginary name and address; And is tested for recalling known historical facts.

Fluency; in the fluency test, we give the patient a letter and ask him to make as many words as he can with that letter. And also in the other section names the animals (each in 1 minute)

Language; The patient is asked to write a series of sequential body instructions using pencil and paper, such as "Put the paper on top of the pencil", to write two complete sentences in terms of instructions, repeating several polynomial words and two short words. Do proverbs for objects shown in 12 drawings, lines and answer textual questions about some objects. Also, read words with irregular and non-smooth pronunciation.

Visuospatial; visual-spatial abilities are tested by asking the patient to copy two diagrams, draw a clock face with the hands set at a specific time, count a set of points, and recognize four scattered letters.

Findings

In this study, 309 patients recovered from COVID-19 with a mean age of 44.90±9.45 years (range 21 to 59) participated. Most of the participants were women (57%). The age groups of 41 to 50 years (35%) and over 50 years (33.3%) had the highest frequency. The level of education of most people was diploma (39.2%). Also, 56% of people were employed. They were.In addition, 25 patients (8.1%) admitted to being intubated during treatment.

According to the findings of Table 1, the average cognitive function of individuals, in general, was 88.86 7 7.26, which achieved about 89% of the total score (100 points) and shows that the majority of people had a normal cognitive function.

The results of Table 2 show that the rate of cognitive function (and all its components) is significantly related to the variables of age, education, and employment of individuals so that with increasing of age, cognitive function decreases; Cognitive performance of people who had a university education level was significantly higher than the other, and also the rate of cognitive performance of employed people was significantly higher than non-employed people. In addition, the rate of cognitive function (and all its components except language) was significantly lower in people who were intubated than in those who were not intubated during treatment.

Overall, based on the Addenbrooke test and its cutoff point, approximately 6% of people who recovered from COVID-19 disease had cognitive problems.

According to Table 3, cognitive function status has a significant relationship with age and intubation ($p<0.05$), so that with increasing age, the frequency of abnormal cognitive function in individuals increases and also the frequency of abnormal cognitive function in People who were intubated (37.5%) were significantly more likely than those who were not intubated (5%).

Table 1) The Mean and standard deviation of cognitive function and its components in patients improved from COVID -19 in 2020

Cognitive function	Mean±SD (min-max)
Attention and orientation	16.1±71.62 (10-18)
Memory	21.2±30.29 (12-26)
Fluency	10.2±28.11 (2-18)
Expressive language	25.1±28.48 (18-26)
Visual-spatial ability	15.1±23.44 (6-16)
Total score	88.7±86.26 (55-100)

Table 2) The Mean and standard deviation of cognitive function components in individuals improved from COVID -19 based on demographic variables

Variables	Attention and orientation	Memory	Fluency	Expressive language	Visual-spatial ability	Total score
Gender						
Male	16.1±89.51	21.2±35.20	10.2±35.12	25.1±37.34	15.1±20.53	89.6±13.78
Female	16.1±58.68	21.2±27.36	10.2±23.10	25.1±21.57	15.1±26.37	88.7±65.61
p-value	0.098	0.744	0.620	0.347	0.725	0.560
Age (Year)						
20-30	17.0±89.87	22.1±17.58	11.1±55.95	25.0±93.37	15.0±72.70	92.3±96.42
31-40	17.1±13.19	21.1±98.94	10.1±74.99	25.1±51.21	15.0±58.97	90.5±93.56
41-50	16.1±60.58	21.2±27.11	10.1±05.93	25.1±32.38	15.1±37.21	88.6±70.63
Over 50 years	16.1±30.97	20.2±64.65	9.2±86.23	24.1±91.81	14.1±73.88	86.8±47.70
p-value	0.000	0.000	0.000	0.003	0.000	0.000
Education level						
Secondary	16.1±47.63	20.2±89.25	10.1±22.86	25.1±07.58	14.1±85.60	87.7±45.19
Diploma	16.1±56.63	21.2±10.11	9.1±23.68	25.1±17.47	15.1±22.47	87.6±48.55
Academic	17.1±28.46	2212±20.39	12.1±01.92	25.1±75.23	15.0±79.89	92.6±97.89
p-value	0.001	0.000	0.000	0.004	0.000	0.000
Occupational status						
Employed	17.1±00.47	21.2±54.19	10.2±57.23	25.1±46.32	15.1±44.13	90.6±03.89
Non employed	16.1±34.72	21.2±00.39	9.1±92.88	25.1±06.63	14.1±97.73	87.7±36.46
p-value	0.000	0.038	0.006	0.020	0.006	0.001
Intubation						
Yes	15.2±04.17	19.3±16.18	8.2±36.41	24.2±48.26	14.2±28.15	81.11±32.28
No	16.1±86.48	21.2±49.10	10.2±45.00	25.1±35.37	15.1±32.33	89.6±52.41
p-value	0.000	0.001	0.000	0.068	0.025	0.001

Table 3) Distribution of cognitive function status in individuals improved by COVID-19 based on demographic variables

Variables	Normal N (%)	Abnormal N (%)	p-value
Gender			
Male	107 (93.9)	7 (6.1)	0.823
Female	133 (92.4)	11 (7.6)	
Age (Year)			
20-30	28 (100)	0	0.036
31-40	62 (96.9)	2 (3.1)	
41-50	82 (94.3)	5 (5.7)	
Over 50	68 (86.1)	11 (13.9)	
Education level			
Secondary	74 (92.5)	6 (7.5)	0.419
Diploma	92 (91.1)	9 (8.9)	
Academic	74 (96.1)	3 (3.9)	
Occupational status			
Employed	147 (94.2)	9 (5.8)	0.489
Non employed	9 (8.8)	93 (91.2)	
Intubation			
Yes	10 (62.5)	6 (37.5)	0.000
No	230 (95.0)	12 (5.0)	

Discussion

This study aimed to evaluate the cognitive function of people with improved COVID-19 disease in 2021. Based on the findings, in general, 5.8% of people had an abnormal cognitive function, which indicates the existence of cognitive problems even after recovery from COVID- 19 disease.

Jaywant's study about the cognitive evaluation of patients recovering from COVID-19 shows that 81% of them had pathology and attention and executive function had impaired in patients who needed acute rehabilitation before discharge [17].

Zhou's study about cognitive function in improved patients with COVID-19 suggests that there is also cognitive dysfunction in improved patients that may be associated with underlying inflammatory processes [16].

According to the Miskawiak study, between 59% and 65% of patients had pathology in terms of verbal learning and executive function. More than 80% of patients had severe cognitive problems in daily life. Objective cognitive impairments were more associated with more subjective cognitive problems and poor quality of life. Poor lung function and more respiratory symptoms after recovery were associated with more cognitive impairments[19]. These Studies in agreement with the present study confirm the existence of cognitive impairment in improved people from COVID-19.

The difference between the rate of abnormal cognitive function in this study and other studies can be because in previous studies were used the recorded information of patients in the acute phase of the disease and hospitalized patients, but in the present study, patients have been evaluated one month after discharge and by eliminating the side effects of drugs and eliminating comorbid disorders such as anxiety and depression and other psychiatric disorders that interfere with cognitive function and eliminating the complications of the acute phase of the disease. Also, in each study has been used of different screening tools.

There is much evidence that COVID- 19 can damage the brain [3, 4, 6, 13, 20-22]. Covid-19 neurological symptoms include stroke, encephalopathy, encephalitis, and peripheral neurological disorders. About 30% of patients with neurological and cognitive symptoms have problems such as attention deficit, executive function, short-term memory, and psychomotor processing [3, 5, 21, 22].

It is not yet known if these symptoms are due to a direct attack of the virus on nerve tissue or as a result of brain damage caused by low oxygen levels or a severe immune reaction known as a cytokine storm. Some evidence suggests that the hippocampus Memory is involved and is vulnerable to COVID-19-related damage. 25 This may explain the persistent memory impairment in COVID- 19 survivors, although these symptoms are rare and are more common in patients with acute respiratory distress syndrome. They need mechanical ventilation or are admitted to the ICU [6, 23].

Cognitive dysfunction in patients with viral infections has been reported in previous studies [16].For example, a study that assessed the effect of virus factors on cognitive function in 347 people with positive immunodeficiency and 395 people seronegative adult Cameroonians showed that people with the virus had problems with attention, learning, and memory function [24]. Another study showed that the Zika virus had a significant effect on neurodevelopmental outcomes including cognitive impairment [25].

In this study, the mean cognitive function of patients was significant in the sub-scales such as attention and orientation, memory, fluidity, expressive language, Visuospatial ability based on age, education, employment, so that with increasing of age, education level, unemployment, cognitive function decreased.

Many studies show that low education is associated with a high prevalence of cognitive impairment [26-29]. Several epidemiological studies have attempted to determine whether low education can increase the risk of cognitive disorders, including dementia. Most reports have reported an inverse relationship between dementia and education level [30-36]. A limited number of studies did not find a relationship between age and education and cognitive disorders [37-39]. Terry et al. showed that there is a relationship between younger age and higher education and a higher rate of cognitive disorders [40].

Three possible mechanisms may explain the higher rate of cognitive impairment in people with lower levels of education. First, people with lower education are more exposed to central nervous system damage (illness, injury or trauma, lack of diet, etc.). Second, people with higher education may have greater nerve storage capacity or a reduced risk of injury. Have nerves. Third, people with higher education may be better able to develop compensatory strategies at both behavioral and neurological levels, and there may also be an interaction between these factors. The above hypotheses cannot be proven because the studies have been performed with different instruments to screen for cognitive disorders, and most studies have been cross-sectional and have not examined better clarification of the dimensions of the disease over time [41].

According to Leibovici's study, education can have a significant effect on changes in secondary memory and language performance, but in other studies, age has been reported as a more important factor. It seems that people with older age and education are more resistant to change in tests with high learning content, i.e. language, and secondary memory tests. The results also show that cognitive functions such as attention, implicit memory, and visual analysis, which may be considered to be higher than "educational" content, seem to make a relatively small difference in the rate of change over time [41].

There is a decrease in age-related cognitive function in some mental functions, such as verbal ability, some numerical abilities, and general information. But other mental abilities decline from middle age or even earlier [42, 43].

In this study, in addition to the above findings, cognitive function and all its components except expressive language were significantly reduced in intubated individuals. The Pandharipande study showed that in critical illnesses, patients admitted to the ICU were at higher risk of cognitive impairment. Their cognitive function scores were similar to those of Alzheimer's patients [12].

The nature of COVID- 19 disease and behavioral limitations such as quarantine and disconnection from family and friends impose varying levels of isolation and stress. The effects of various stressors on cognitive function in various areas such as risk perception, working memory, attention, decision making, problem-solving, and emotion control have been proven. To improve people's cognitive biases and control their fear and stress, we suggest that paid attention to cognitive rehabilitation. The first step is to develop a critical mindset to find fake news because fake news targets one's emotions. Breaking fake news is an effective step to reduce the spread of fear and anxiety. The second step is to develop a positive intervention approach to control and accept them. In addition, other interventions such as cognitive-behavioral therapy and cognitive rehabilitation should be considered as useful interventions to recognize the importance of cognitive deficits.

Conclusion

In general, the findings showed that cognitive impairment there are after improving from COVID-19 disease and patients with lower education and older age and patients undergoing intubation were at higher risk of cognitive impairment. It is suggested Cognitive function be evaluated after the disease in the long term.

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Ethical Permissions: The present study was conducted after obtaining permission from the ethics committee of Kashan University of Medical Sciences with number IR.KAUMS.MEDENT.REC.1399.181.Written consent was obtained from the participants and the questionnaires were reviewed anonymously.

Conflicts of Interests: None declared.

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