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Cognitive impact on patients with COVID-19 infection

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Abstract

Background SARS-COV-2 infection reframed medical knowledge in many aspects, yet there is still a lot to be discovered. Coronavirus disease 19 (COVID-19) can cause neuropsychiatric, psychological, and psychosocial impairments. Literature regarding the cognitive impact of COVID-19 is still limited.

This study aims to evaluate cognitive function, anxiety, and depression among patients with coronavirus disease 19.

Methods Sixty COVID-19 patients were recruited and sub-grouped according to the site of care into three groups, home isolation, ward, and RICU, and compared with 60 matched control participants. Entire clinical history, O₂ saturation, mini-mental state examination (MMSE), Hamilton's anxiety (HAM-A), and depression rating scales (HAM-D) were assessed.

Results MMSE showed significantly lowest results for the ICU group, with a value of 21.65 ± 3.52 . Anxiety levels were the highest for the ICU group, with a highly significant difference vs. the home isolation group (42.45 ± 4.85 vs. 27.05 ± 9.52 ; p < 0.001). Depression values assessed showed a highly significant difference in intergroup comparison (44.8 ± 6.64 vs. 28.7 ± 7.54 vs. 31.25 ± 8.89 ; p < 0.001, for ICU vs. ward vs. home group, respectively).

MMSE revealed a significant negative correlation with age and education level, anxiety level had significant negative correlations with severity of illness and male gender, and depression level had highly significant negative correlations with severity of illness and male gender.

Conclusion Both cognitive and neuropsychiatric symptoms were affected in COVID-19 cases, especially in ICU-admitted patients. The impact of these disorders was significant in older age, lower oxygen saturation, and severe disease.

Trial registration ClinicalTrials.gov. NCT05293561. Registered on March 24, 2022.

Keywords COVID-19, Cognitive impairment, Anxiety, Depression

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Introduction

COVID-19 results in various symptoms with multiorgan affection, including fever, cough, grave respiratory symptoms, gastrointestinal manifestations, and fatigue [1]. Continuous neurological and psychological evaluation efforts revealed that headache, dizziness, and cerebrovascular events had been frequently reported [2]. Anosmia and ageusia were reported as early indicators of SARS-CoV-2 infection, suggesting that early neurological involvement may be relevant [3].



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Public health emergencies such as COVID-19 are likely to cause adverse neuropsychiatric impacts. Cognitive impairments after SARS-COV-2 infection were noticed, including poor concentration and declined memory as well as insomnia, anxiety, and depression symptoms [4].

The battle against COVID-19 is continuing worldwide. People's adherence to confinement regulations and response to vaccination campaigns is essential and primarily affected by their knowledge, attitudes, and practices toward COVID-19. Home isolation and social distancing are also associated with fear, frustration, anxiety, and depressive symptoms [5].

During the acute phase of COVID-19 infection, about 36% of cases develop neurological symptoms, of which 25% can be attributed to the direct involvement of the central nervous system [6]. Patients who show neurological symptoms included cases with or without pre-existing neurological disorders [7]. In intensive care units, patients showed agitation, confusion, and corticospinal tract signs such as enhanced tendon reflexes and clonus. COVID-19 can further lead to changes in coagulation and, in particular, to inflammation-induced disseminated intravascular coagulation (DIC) [3].

This study aims to evaluate cognitive function, anxiety, and depression among patients with coronavirus disease 19.

Patients and methods

Study participants and design

This prospective cross-sectional case-control study was performed on 60 COVID-19 patients in the age group of 18–70 years who were diagnosed using reverse transcription-polymerase chain reaction (RT-PCR) to confirm the diagnosis of COVID-19 and belonging to either gender. Data of 20 patients recruited from home isolation at the first visit to the outpatient clinic, 20 patients included from the hospital isolation ward, and 20 patients recruited from respiratory isolation ICU, Chest Department of Assiut University Hospital from January 2021 to October 2021.

Based on the Egyptian MOH protocol (version 1.4, Nov 2020) [8], patients were classified into mild, moderate, severe, and critical; hence triaged to receive treatment either at the home, ward, or ICU.

Mild cases were symptomatic cases with lymphopenia or leucopenia with no radiological signs of pneumonia with no risk factors, including age 65, temperature > 38 °C, SaO2 \leq 92%, heart rate \geq 110, respiratory rate \geq 25/min., neutrophil/lymphocyte ratio on CBC \geq 3.1, uncontrolled comorbidities, immunosuppressive drug, pregnancy, active malignancy, on chemotherapy, and obesity (BMI>40).

Moderate showed positive chest radiological finding of pneumonia with oxygen saturation \geq 92%.

Severe cases included patients with either SpO₂ \leq 92% on room air, PaO₂/FiO₂ ratio < 300, or chest CT showing more than 50% lesion.

Critically ill patients have respiratory failure, septic shock, and/or multi-organ dysfunction.

Inclusion criteria

All patients between the ages of 18 and 70 attending the chest department outpatient clinic or admitted to the chest department isolation unit and RICU were eligible for enrollment in the current study.

Exclusion criteria

Age under 18, other end organ failure conditions, previous neurological or psychiatric involvement, disturbed level of consciousness, uncooperative patients or cannot perform the psychometric tests, those who needed MV or sedation, and refusal to sign the consent.

Demographic, clinical, and laboratory data

Included patients underwent careful history taking, and associated comorbidities and the presence of symptoms were recorded. Patients were identified by with international classification of diseases (ICD-10). Comorbidities include diabetes mellitus (DM), hypertension (HTN), moderately to severe renal dysfunction (creatinine > 3mg or renal failure), hepatic dysfunction (viral hepatitis, liver cirrhosis, and hepatic failure), ischemic heart disease (IHD), and heart failure. Radiological assessment by chest computed tomography (CT) was also done to classify the patients according to severity and level of care.

Pulse oximeter saturation

Oxygen saturation was recorded during recruitment (SpO_2) .

Mini-mental state examination (MMSE)

A 30-point test used to assess cognitive function includes tests of orientation, attention, memory, language, and visual-spatial skills. MMSE scores 24–30: no cognitive impairment, 19–23: mild cognitive impairment, 10–18: moderate cognitive impairment, \leq 9: severe cognitive impairment. MMSE is an eleven items test and on average performing the test requires 5–10 min [9, 10].

Hamilton anxiety rating scale (HAM-A)

This consists of 14 items and measures both psychic anxiety (mental agitation and psychological distress) and somatic anxiety (physical complaints related to anxiety). Each item is scored on a scale of 0 (not present) to 4 (severe), with a total score range of 0–56, where a score \leq 17 indicates mild anxiety, 18–24 mild to moderate severity, and more than 24 moderate to severe anxiety. Usually, the test requires 15–20 min for its performance [11, 12].

Hamilton Depression Rating Scale (HAM-D)

The original HAM-D has 21 items, but scoring is based only on the first 17. Scores less than or equal to 7 indicate normal response, 8–13 mild depression, 14–18 moderate, 19–22 severe, and more than 22 very severe depression. On average, the test time is between 15 and 20 min [13–15].

Statistical analysis

Data was collected and analyzed using SPSS (statistical package for social sciences) program (version 24, IBM and Armonk, New York). Continuous data were expressed in the form of the mean (\pm SD) and compared by the Mann-Whitney test and Kruskal-Wallis test for groups of more than two, while nominal data were expressed in the form of frequency (percentage) and compared by the chi-square test. Different correlations of continuous variables in the study were determined with Spearman's correlation.

Sampling and sample size

Sampling was done by non-probability convenient sampling technique. The sample size was estimated by the Open Epi V.3.01 computer program.

Matching and masking

All patients fulfilling inclusion and exclusion criteria were eligible for participation in the study regardless of prognosis or any other factor that may influence the study results. The assessment was done shortly after the initial diagnosis and site of care decision. The control group was selected from age, gender, residence, and educational level matched patients' relatives and healthy volunteers. The neuropsychological studies were performed by a single neuropsychologist who was blinded to patient prognosis and laboratory data upon performing the psychometric studies.

Ethical consideration

All participants or their legal guardians gave informed written consent. The study protocol was approved by the Ethical Committee of the Faculty of Medicine, Assiut University (IRB: 04-2023-300055), and it was carried out under the Declaration of Helsinki with clinical trials ID: NCT05293561.

Results

The current study enrolled 120 personnel; 60 health, age, and sex-matched controls and 60 patients with COVID-19 disease; 20 patients experienced severe illness and received care in the respiratory intensive care unit (RICU)-none of them was MV and five of them required intermittent HFNC; 20 patients were isolated at the ward; and 20 were isolated at home. The mean age of patients was 52.58 ± 17.29 years vs. 47.52 ± 15.05 for the control group. Both groups showed no significant difference regarding baseline data, including gender, smoking, education level, residence, and associated comorbidities (Table 1). Subgroup analysis of recruited patients revealed insignificant differences as regards age, sex, smoking status, education level, and residence (p > 0.05)(Table 2). There was no significant difference between groups regarding comorbidities, including hypertension, diabetes, renal dysfunction, hepatic dysfunction, and cardiac dysfunction (Table 3). Patients with ICU admission as the level of care showed the lowest values regarding oxygen saturation levels of 73.4 ± 12 versus 86.90 ± 3.87 for the ward isolation group and 93.7 ± 2.13 for the home isolation group (Table 3).

Mini-mental state evaluation results showed a significant difference between the ICU group versus the ward group and home isolation group (21.65 ± 3.52 vs. 24.05 ± 3.72 , p=0.01; 21.65 ± 3.52 vs. 24.40 ± 3.4 , p=0.001), respectively (Table 4).

Comparison between the three groups regarding anxiety levels showed a highly significant difference (p< 0.001), also intergroup comparison displayed a significant difference between the ICU group vs. home group and ward group vs. home group (42.45 ± 4.85 vs. 27.05 ± 9.52 & 33.15 ± 9.12 vs. 27.05 ± 9.52), respectively (Table 5).

Comparison between the three groups regarding depression levels showed a highly significant difference (p < 0.001), also intergroup comparison displayed a significant difference between ICU group vs. home group and ward group vs. home group (44.8 ± 6.64 vs. 31.25 ± 8.89 & 28.7 ± 7.54 vs. 31.25 ± 8.89), respectively (Table 6).

Cognitive dysfunction showed a significant positive correlation with SpO₂ level (r=0.283, p=0.029) and a significant negative correlation with age. Anxiety level values had a significant positive correlation with SpO₂ level (r=0.566, p< 0.001) and negative correlations with the severity of illness. Depression level values showed significant positive correlations with SpO₂ level (r=0.546, p< 0.001) and negative correlations (r=0.546, p< 0.001) and negative correlations (Table 7).

	COVID-19 group (<i>n</i> =60)	Control group (<i>n</i> =60)	P value
Sex			
Male	32 (53%)	44 (73%)	0.067
Female	28 (47%)	16 (27%)	
Age (years)			
Mean ± SD	52.58 ± 17.29	47.52 ± 15.05	0.09
Smoking			
Smoker	14 (23.3%)	26 (43%)	0.078
Ex-smoker	8 (13.3%)	9 (15%)	
Non-smoker	38 (63.3%)	25 (42%)	
Education			
Literate	46 (77%)	52 (87%)	0.238
Illiterate	14 (23%)	8 (13%)	
Residence			
Urban	10 (17%)	17 (28%)	0.189
Rural	50 (43%)	43 (72%)	
Diabetes			
Non-diabetic	42 (70%)	52 (87 %)	0.063
Diabetic	18 (30%)	8 (13%)	
Hypertension			
Not hypertensive	43 (72%)	46 (77%)	0.463
Hypertensive	17 (28	14 (23%)	
SpO ₂			
Mean ± SD	84.67 ± 11.18	98.45 ± 0.83	<0.001*
MMSE			
Mean ± SD	22.98 ± 3.95	27.62 ± 1.76	<0.001*
HAM-A			
Mean ± SD	34.22 ± 10.21	8.36 ± 3.77	<0.001*
HAM-D			
Mean ± SD	34.92 ± 10.42	7.12 ± 3.93	< 0.001*

Table 1 Demographic data of the studied COVID-19 patients versus the control group

Continuous data were expressed as mean (\pm SD) and compared by Mann-Whitney test, while nominal data were expressed in frequency (percentage) and compared by χ^2 tests

COVID-19 coronavirus disease 2019, SpO₂ saturation of peripheral oxygen, MMSE mini-mental state examination, HAMA-A Hamilton anxiety scale, HAMA-D Hamilton depression rating scale. * indicates a highly significant p-value

Discussion

Generally, the exact prevalence of cognitive and psychological disturbances in COVID-19 disease is unknown. It varies considerably across studies, which can be explained by the different neurological and psychological tests used in different studies.

Our study detected moderate to severe cognitive impairment in nearly 13% of the study group, severe anxiety in nearly 81%, and severe level of depression in nearly 88% of patients.

Neuropsychiatric affection in the course of SARS-COV-2 has been described in many studies [6, 7]. The pathophysiology of such involvement has been described due to different etiologies. Theories include direct viral invasion of neurons, affection of vascular endothelium, affection of the blood-brain barrier, and increased coagulation state. Also, some neurological conditions have been reported to be closely associated with SARS-COV-2 infection, such as Guillain-Barre syndrome, peripheral neuritis, and encephalopathy [16–18]. Cognitive impairment can partly be explained by admission to the intensive care unit in critical illness [19].

In a study by Egbert et al. on COVID-19 patients, many cerebral abnormalities were described in 34% of patients as white matter hyperintensities, cerebral hemorrhage, and infarction [20].

Neuro-inflammation reported in COVID-19 patients could be a pathogenesis to neurocognitive impairment in

Table 2 Comparison between demographic data of the studied patients with different sites of care

	ICU group (<i>n</i> =20)	Ward group (<i>n</i> =20)	Home isolation (n=20)	P1	P2	P3	P4
Gender							
Male	13 (65%)	8 (40%)	11 (55%)	0.205	0.748	0.527	0.206
Female	7 (35%)	12 (60%)	9 (45%)				
Age (years)							
Mean ± SD	51.55 ± 15.9	53.55 ± 16.82	52.65 ± 19.74	0.919	0.283	0.288	0.937
Smoking							
Smoker	8 (40%)	2 (10%)	4 (20%)	0.074	0.658	0.565	0.239
Ex-smoker	1 (5%)	3 (15%)	4 (20%)				
Non-smoker	11 (55%)	15 (75%)	12 (60%)				
Education							
Literate	15 (75%)	17 (85%)	14 (70%)	0.695	0.723	0.225	0.521
Illiterate	5 (25%)	3 (15%)	6 (30%)				
Residence							
Urban	3 (15%)	4 (20%)	3 (15%)	0.5	0.669	0.5	0.887
Rural	17 (85%)	16 (80%)	17 (85%)				

Continuous data were expressed in the form of the mean (\pm SD) and compared by the Mann-Whitney test and Kruskal-Wallis test for groups of more than two, while nominal data were expressed in the form of frequency (percentage) and compared by χ^2 tests

P1 P value between ICU and ward groups, P2 P value between ICU and home isolation group, P3 P value between ward and home isolation groups, P4 P value between the three groups

Table 3 Comorbidities and SpO₂ level of the studied patients based on the severity of illness and site of care

ICU group (n=20)	Ward group (n=20)	Home isolation	P1	P2	P3	P4	
J S S S S S S S S S S	J J J J J	(<i>n</i> =20)					
16 (80%)	15 (75%)	17 (85%)	0.653	0.681	0.677	0.061	
4 (20%)	5 (25%)	3 (15%)					
17 (85%)	17 (85%)	18 (90%)	0.669	0.632	0.632	0.645	
3 (15%)	3 (15%)	2 (10%)					
18 (90%)	19 (95%)	18 (90%)	0.5	0.698	0.545	0.069	
2 (10%)	1 (5%)	2 (10%)					
13 (65%)	16 (80%)	13 (65%)	0.240	0.629	0.288	0.154	
7 (35%)	4 (20%)	7 (35%)					
16 (80%)	14 (70%)	13 (65%)	0.653	0.288	0.325	0.431	
4 (20%)	6 (30%)	7 (35%)					
73.4 ± 12	86.90±3.87	93.7 ± 2.13	0.002*	<0.001*	0.003*	<0.001*	
5 (25%)							
	ICU group (<i>n</i> =20) 16 (80%) 4 (20%) 17 (85%) 3 (15%) 18 (90%) 2 (10%) 13 (65%) 7 (35%) 16 (80%) 4 (20%) 73.4 ± 12 5 (25%)	ICU group (n=20) Ward group (n=20) 16 (80%) 15 (75%) 4 (20%) 5 (25%) 17 (85%) 17 (85%) 3 (15%) 17 (85%) 3 (15%) 3 (15%) 18 (90%) 19 (95%) 2 (10%) 16 (80%) 7 (35%) 4 (20%) 16 (80%) 14 (70%) 4 (20%) 6 (30%) 73.4 \pm 12 86.90 \pm 3.87 5 (25%)	ICU group (n=20)Ward group (n=20)Home isolation (n=20)16 (80%)15 (75%)17 (85%)4 (20%)5 (25%)3 (15%)17 (85%)17 (85%)18 (90%)3 (15%)3 (15%)2 (10%)18 (90%)2 (10%)18 (90%)2 (10%)19 (95%)18 (90%)2 (10%)1 (5%)2 (10%)13 (65%)16 (80%)13 (65%)7 (35%)4 (20%)7 (35%)16 (80%)14 (70%)13 (65%)4 (20%)6 (30%)7 (35%)73.4 \pm 1286.90 \pm 3.8793.7 \pm 2.135 (25%)	ICU group (n=20)Ward group (n=20)Home isolation (n=20)P116 (80%)15 (75%)17 (85%)0.6534 (20%)5 (25%)3 (15%)0.66917 (85%)17 (85%)18 (90%)0.6693 (15%)3 (15%)2 (10%)0.66918 (90%)19 (95%)18 (90%)0.52 (10%)19 (95%)18 (90%)0.52 (10%)19 (95%)18 (90%)0.513 (65%)16 (80%)13 (65%)0.2407 (35%)14 (70%)13 (65%)0.6534 (20%)6 (30%)7 (35%)0.65373.4 ± 1286.90±3.87 93.7 ± 2.13 0.002*5 (25%)	ICU group (n=20)Ward group (n=20)Home isolation (n=20)P1P216 (80%)15 (75%)17 (85%)0.6530.6814 (20%)5 (25%)3 (15%)0.6690.63217 (85%)17 (85%)18 (90%)0.6690.6323 (15%)3 (15%)2 (10%)0.50.69818 (90%)19 (95%)18 (90%)0.50.6982 (10%)19 (95%)18 (90%)0.50.69813 (65%)16 (80%)13 (65%)0.2400.6297 (35%)4 (20%)7 (35%)0.6530.2884 (20%)6 (30%)7 (35%)0.6530.28873.4 ± 1286.90±3.8793.7 ± 2.130.002*<0.001*	ICU group (n=20)Ward group (n=20)Home isolation (n=20)P1P2P316 (80%)15 (75%)17 (85%)0.6530.6810.6774 (20%)5 (25%)3 (15%)0.6690.6320.63217 (85%)17 (85%)18 (90%)0.6690.6320.6323 (15%)2 (10%)0.50.6980.54518 (90%)19 (95%)18 (90%)0.50.6980.5452 (10%)19 (95%)13 (65%)0.2400.6290.2887 (35%)16 (80%)13 (65%)0.2400.6290.2887 (35%)14 (70%)13 (65%)0.6530.2880.3254 (20%)6 (30%)7 (35%)0.002*<0.001*	

Continuous data were expressed in the form of the mean (\pm SD) and compared by the Mann-Whitney test and Kruskal-Wallis test for groups of more than two, while nominal data were expressed in the form of frequency (percentage) and compared by χ^2 tests. The *P* value was significant if < 0.05

P1P value between ICU and ward groups, P2P value between ICU and home isolation group, P3P value between ward and home isolation groups, P4P value between the three groups, * indicates a highly significant p-value

covid-19 patients [21]. Altered host immune response and cytokine storm syndrome is another key factor for cognitive impairment in the course of illness [22]. Increased level

of cytokine interleukins (IL)-1ß has been linked to the presence of depression and anxiety in COVID-19 patients than those with normal (IL)-1ß level [23, 24].

Table 4 Mini-mental state evaluation results of the studied patients based on the severity of illness and site of care

Groups	ICU group (<i>n</i> =20)	Ward group (<i>n</i> =20)	Home isolation	P1	P2	P3	P4
		(<i>n</i> =20)					
MMSE							
Mean ± SD	21.65 ± 3.52	24.05± 3.72	24.40±3.4	0.01*	0.001*	0.769	0.043
Normal				0.006*			
MMSE ≥ 24	7 (35%)	11 (55%)	14 (70%)				
Mild impairment							
MMSE 19-23	8 (40%)	8 (40%)	4 (20%)				
Moderate to severe							
MMSE≤ 18	5 (25%)	1 (5%)	2 (10%)				

Continuous data were expressed in the form of the mean (\pm SD) and compared by the Mann-Whitney test and Kruskal-Wallis test for groups of more than two, while nominal data were expressed in the form of frequency (percentage) and compared by χ^2 tests. The *P* value is significant if < 0.05

P1 P value between ICU and ward groups, P2 P value between ICU and home isolation group, P3 P value between ward and home isolation groups, P4 P value between the three groups, MMSE mini-mental state examination. * indicates a highly significant p-value

Table 5 Hamilton anxiety rating scale results of the studied patients based on the severity of illness and site of care

Groups	ICU group (<i>n</i> =20)	Ward group (<i>n</i> =20)	Home isolation (<i>n</i> =20)	P1	P2	P3	P4
HAM-A							
Mean ± SD	42.45 ± 4.85	33.15 ± 9.12	27.05±9.52	0.240	<0.001*	0.003*	<0.001*
Mild anxiety				0.002*			
≤ 17	0 (0%)	1 (5%)	3 (15%)				
Moderate anxiety	,						
18–24	0 (0%)	3 (15%)	4 (20%)				
Severe anxiety							
>24	20 (100%)	16 (80%)	13 (65%)				

Continuous data were expressed in the mean (\pm SD) and compared by the Mann-Whitney test and Kruskal-Wallis test for groups of more than two, while nominal data were expressed in frequency (percentage) and compared by χ^2 tests. *P* value was significant if < 0.05

P1 P value between ICU and ward groups, P2 P value between ICU and home isolation group, P3 P value between ward and home isolation groups, P4 P value between the three groups, HAMA-A Hamilton anxiety rating scale. *indicates a highly significant p-value

Table 6	Hamilton depression	rating scale results of t	ne studied patients based	d on the severity of illness	and site of care
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Groups	ICU group (n=20)	Ward group (<i>n</i> =20)	Home isolation group (<i>n</i> =20)	P1	P2	P3	P4
HAM-D			5 1 1 7				
Mean ± SD	44.8 ± 6.64	28.7 ± 7.54	31.25±8.89	0.866	<0.001*	<0.001*	<0.001*
Normal				0.117			
≤ 7	0 (0%)	0 (0%)	0 (0%)				
Mild-moderate							
8–18	0 (0%)	3 (15%)	4 (20%)				
Severe							
≥ 19	20 (100%)	17 (85%)	16 (80%)				

Continuous data were expressed in the form of the mean (\pm SD) and compared by the Mann-Whitney test and Kruskal-Wallis test for groups of more than two, while nominal data were expressed in the form of frequency (percentage) and compared by χ^2 tests. The *P* value was significant if < 0.05

P1 P value between ICU and ward groups, P2 P value between ICU and home isolation group, P3 P value between ward and home isolation groups, P4 P value between the three groups, HAMA-D Hamilton depression rating scale. * indicates a highly significant p-value

	MMSE		HAM-A		HAM-D	
	<i>r</i> value	P value	r value	P value		
Severe disease	0.167	0.203	-0.621	<0.001*	-0.535	<0.001*
SaO ₂	0.283	0.029*	0.566	<0.001*	0.546	<0.001*
Age	-0.574	<0.001*	0.304	0.056	0.068	0.678

Table 7 Correlation of MMSE, HAM-A, and HAM-D values with other parameters in the study COVID-19 group (n=60)

The correlation for variables in the study was determined with Spearman's correlation. r correlation coefficient rho. P value was significant if < 0.05

SaO₂ oxygen saturation, MMSE mini-mental state examination, HAM-A Hamilton anxiety rating scale, HAM-D Hamilton depression rating scale. * indicates a highly significant p-value

Wang et al. enrolled a sample of young adults with COVID-19 affection; psychological impairment was present in more than 50% of the study group, with moderate to severe impairment [25].

In agreement with our results, Mazza and colleagues enrolled a group of young adults affected with COVID-19 infection in assessing stress levels. They reported high to very high-stress levels in 29% of them [26].

The duration and extent of neuropsychiatric affection during SARS-COV-2 are still debated in the literature. Still surprisingly, some studies reported the persistence of symptoms for more than 2 months after the SARS-COV-2 infection had been resolved [27]. Even the expression long COVID has been used in literature [28].

Surprisingly, Huang and colleagues' study in a group of COVID-19 survivors from Wuhan reported some neuropsychiatric manifestations after 6 months of acquiring a SARS-COV-2 infection, including muscular weakness, easy fatigability, anxiety, and depression [28].

In agreement with our study, Morin et al. enrolled 478 COVID-19 patients after the resolution of infection. They reported cognitive impairment in 21% of them; such symptoms were absent before infection, 177 patients were hospitalized, and they detected the presence of cognitive impairment using the MoCA score in 38% of them [29].

Mattioli et al., studying the cognitive impairment in COVID-19 patients in 120 patients and 30 age and sexmatched control, observed memory difficulties in 6.6 % of patients and irritability and anxiety in 5 % of patients. Using neurophysiological tests' scores and DASS scores, specifically MMSE, was slightly impaired compared to the control group but with no significant difference. At the same time, there were significant differences between the two groups in DASS-21 anxiety, stress, and depression scores [30].

We attribute the difference between results in MMSE to the difference in the study group in which Mattioli et al. study group were all well-educated, healthy coworkers and only two patients were admitted to the ICU, and 97.6% of his study group did not need oxygen therapy. They related the absence of significant difference due to the selection of mild to moderate cases of COVID-19 patients [30].

In agreement with our results, Schou et al., in an important meta-analysis using data from 66 studies, reported that the most frequent psychiatric impairments were depression and anxiety and closely linked to the severity of disease and duration of hospitalization and that symptoms persist after the resolution of the infection. Also, baseline comorbidities are an essential factor in developing anxiety and depression. He also reported that cognitive decline is present in 27 studies, including deficits in attention, memory, and concentration [31].

In another meta-analysis by Badenoch et al., 51 studies were eligible to be enrolled in his analysis with the sum of 18,917 participants; depression was found in 12.9% of patients, anxiety in 19.1% of patients, and 20.2% showed cognitive impairment [32].

Hu et al. studied 85 inpatients with COVID-19 affection; 45.9% were affected with depression, 21.2% with mild, 50.3% with moderate, and 8% with severe depression. Anxiety was found in 37.8% of patients; 22.4% mild, 11.8% moderate, and 4.7% expressed severe anxiety. Kong et al. studied 144 patients, using the hospital anxiety and depression scale; anxiety and depression were found in 34.7% and 28.4% of patients, respectively [23].

In agreement with our results, Khanal and his colleagues who enrolled 372 home-isolated COVID-19 patients reported that 52.7% of the study group had borderline depression and 26.3% had manifest depression. They contributed to the significant level of depression among home-isolated patients that exceed the centrally isolated patient in some literature to COVID-19-related symptoms, fear of deterioration, and lack of medical care [33]. Another study by Gao et al demonstrated that exposure to social media and the outbreak news was associated with a high level of depression [34].

We must acknowledge the following limitations to our study: the study is single-centered; thus, results could not be generalized due to socio-demographic variabilities. Although cognitive affection anxiety and depression associated with COVID-19 infection are reported in many studies, the etiological bases beneath are still not fully studied; the manifestations are multifactorial and could be related to the disease itself, medication, and/or ICU admission.

Conclusion

Cognitive impairment, anxiety, and depression are common findings in COVID-19 patients and are directly proportional to the severity of illness, oxygen saturation, and age. We recommend continuous observation of those impairments in COVID-19 patients, especially critically ill patients. We encourage further research to alleviate those symptoms and decrease the burden of those impairments through SARS-COV-2 infection.

Abbreviations

COVID-19	Coronavirus disease 2019
СТ	Computed tomography
DASS	Depression Anxiety and Stress Scale
DIC	Disseminated intravascular coagulation
DM	Diabetes mellitus
FiO ₂	Fraction of inspired oxygen
HAMA-A	Hamilton anxiety rating scale
HAMA-D	Hamilton Depression rating scale
HTN	Hypertension
ICU	Intensive care unit
IL	Interleukin
MoCA	Montreal cognitive assessment
MOH	Ministry of Health
MMSE	Mini-mental state examination
PaO ₂	Arterial pressure of oxygen
RICU	Respiratory intensive care unit
RT-PCR	Reverse transcription-polymerase chain reaction
SARS-COV-2	Severe acute respiratory syndrome coronavirus 2
SPO ₂	Saturation of peripheral oxygen
SPSS	Statistical Package for Social Sciences

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Authors' contributions

AMS, AARMH, AMAT, and WGEK: conception and design. AMS, AMAT, and WGEK: data collection. AMS and WGEK: statistical analysis. AMS, AARMH, AMAT, and WGEK: medical writing. The authors revised the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the institutional review board and ethical committee of the Faculty of Medicine, Assiut University, in compliance with the Helsinki Declaration (IRB: 04-2023-300055).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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