Cognitive and Neuropsychiatric Impairments Associated With COVID-19 In Patients Evaluated in Brazil

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BACKGROUND

Neurological and neuropsychiatric impairments after COVID-19 have been described since the beginning of the pandemic, particularly cognitive impairment, commonly referred to as brain fog, and deficits in attention, executive function, language, processing speed, and memory are the most common symptoms. Our objective is to evaluate cognitive and neuropsychiatric impairments in patients who presented neurological manifestations associated with COVID-19.

METHODS

Prospective, longitudinal, observational study designed to compare cognitive performance in patients after COVID-19 over a six-month interval, also considering the presence of cognitive complaints. The study was conducted between September 2020 and February 2023 at Institute of Infectious Diseases “Emílio Ribas” and included patients aged 18 to 65 years without a history of neurological or psychiatric disorders, excluding individuals with fewer than four years of education. Cognitive tests were administered at three points in the study, 0-3-6 months, and cognitive impairment was defined in patients who presented alterations in the revised Addenbrooke’s Cognitive Examination (ACE-R) and in the Mini-Mental State Examination. The Beck Anxiety and Depression Inventories were administered, and neuropsychiatric alteration was defined in patients with moderate or severe levels of anxiety and depression. Analysis of inflammatory markers was performed in serum and cerebrospinal fluid (CSF).

Cognitive and neuropsychiatric impairments occur after COVID-19, even in the absence of self-reported cognitive complaints.

RESULTS

Table 1 - Sociodemographic and clinical profile of patients at study entry.

Variables	Group: With cognitive complaint, n (%) n= 41 (70.7)	Group: Without cognitive complaint, n (%) n= 17 (29.3)	Total, n (%) n= 58 (100)	p-value
Gender				0.283
Female	30 (73.2)	10 (58.8)	40 (69.0)	
Male	11 (26.8)	7 (41.2)	18 (31.0)	
Age (years)				0.073
18-50	22 (53.7)	14 (82.4)	36 (62.1)	
51-65	19 (46.3)	3 (17.6)	22 (37.9)	
Age (years) Mean (SD)	48.3 (9.4)	40.6 (8.7)	46.1 (9.8)	**0.005**
Median	47.0	38.0	45.5	
Years of education				
≥ 12	28 (68.3)	11 (64.7)	39 (67.2)	0.791
4-11	13 (31.7)	6 (35.3)	19 (32.8)	
Years of education Mean (SD)	14.6 (4.0)	13.2 (3.4)	14.2 (3.9)	0.260
Median	16.0	14.0	15.0	

Table 2 - Univariate analysis of cognitive impairment at study entry.

Variables	Present cognitive impairment, n (%) n= 29 (50)	Absent cognitive impairment, n (%) n= 29 (50)	OR (95% CI)	p-value
Gender			1.921	0.256
Female, n= 40	22 (75.9)	18 (62.1)	(0.618;5.970)	
Male, n= 18	7 (24.1)	11 (37.9)		
Age (years)			1.341	0.588
18-50, n= 36	17 (58.6)	19 (65.5)	(0.463;3.887)	
51-65, n= 22	12 (41.4)	10 (34.5)		
Years of education			1.170	0.780
≥ 12, n= 39	20 (69.0)	19 (65.5)	(0.390;3.506)	
4-11, n=19	9 (31.0)	10 (34.5)		
Anxiety			3.109	**0.036**
Absent or mild, n= 30 (51.7%)	11 (37.9)	19 (65.5)	(1.064;9.081)	
Moderate or severe, n= 28 (48.3%)	18 (62.1)	10 (34.5)		
Depression			0.799	0.738
Absent or mild, n= 47 (81.0%)	24 (82.8)	23 (79.3)	(0.214;2.982)	
Moderate or severe, n= 11 (19.0%)	5 (17.2)	6 (20.7)		
Cognitive complaint			1.181	0.773
Present, n= 41	21 (72.4%)	20 (69.0)	(0.381;3.665)	
Absent, n= 17	8 (27.6)	9 (31.0)		

Table 3 - Performance in ACE-R domains in patients with cognitive impairment

ACE-R domains	Present cognitive impairment, n (%) n= 29
Attention and orientation	
Altered, n= 24	21 (72.4)
Normal, n= 34	8 (27.6)
Memory	
Altered, n= 40	24 (82.8)
Normal, n= 18	5 (17.2)
Verbal fluency	
Altered, n= 30	17 (58.6)
Normal, n= 28	12 (41.4)
Language	
Altered, n= 38	23 (79.3)
Normal, n= 20	6 (20.7)
Visuospatial skills	
Altered, n= 28	20 (69.0)
Normal, n= 30	9 (31.0)

Abbreviation: ACE-R: Addenbrooke's Cognitive Examination – Revised Version

Table 4 - Univariate analysis of neuropsychiatric impairment at study entry.

Variables	Present neuropsychiatric impairment, n (%) n= 33 (56.9)	Absent neuropsychiatric impairment, n (%) n= 25 (43.1)	OR (95% CI)	p-value
Gender			0.553	0.313
Female, n= 40	21 (63.6)	19 (76.0)	(0.173;1.763)	
Male, n= 18	12 (36.4)	6 (24.0)		
Age (years)				
18-50, n= 36	22 (66.7)	14 (56.0)	0.636	0.407
51-65, n= 22	11 (33.3)	11 (44.0)	(0.218;1.857)	
Years of education			2.455	0.112
≥ 12, n= 39			(0.800;7.536)	
4-11, n=19	25 (75.8)	14 (56.0)		
	8 (24.2)	11 (44.0)		
Cognitive complaint			0.632	0.439
Present, n= 41	22 (66.7)	19 (76.0)	(0.196;2.033)	
Absent, n= 17	11 (33.3)	6 (24.0)		

CONCLUSIONS

The main conclusions of our study were:

1) Cognitive and neuropsychiatric changes are associated with COVID-19, with prevalences of 50% and 56.9%, respectively, at baseline. There was an improvement in cognitive test scores over the six months of evaluation, but not enough to reach normality;

2) The most affected cognitive domains were attention and orientation, memory, language, and visuospatial skills, and there was persistence of cognitive impairment and a decrease in the prevalence of moderate and severe anxiety and depression in our sample throughout the study;

3) The most relevant clinical association was that moderate or severe anxiety increases the risk of cognitive impairment, and we did not observe risk factors for neuropsychiatric impairment;

4) There was no significant association between biomarkers of neural degeneration, cytokines, and chemokines in CSF and serum with cognitive impairment.

ADDITIONAL KEY INFORMATION

I thank the patients for their dedicated participation in the study and the entire NeuroCovBR study group for carrying out work of national importance for Brazil.

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Cognitive complaints were not predictive of cognitive impairment in this study, and there is a difference between the patient's perception of their symptom and what cognitive tests show regarding cognitive decline.