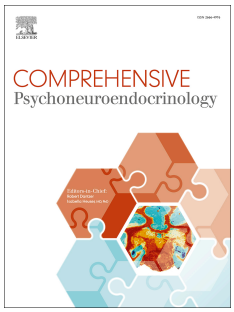

Coronavirus Disease 2019 and its Impact on the Cognition of Older Adults: Unraveling the Role of Inflammation

Shahrzad Mortazavi, Vahid Rashedi, Bahman Cheraghian, Fatemeh Pourshams, Saeid Saeidimehr, Bahram Dehghan, Maryam Pourshams

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Coronavirus Disease 2019 and its Impact on the Cognition of Older Adults: Unraveling the Role of Inflammation

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Coronavirus Disease 2019 and Cognition of Older Adults

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Running title: Coronavirus Disease 2019 and Cognition of Older Adults

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ABSTRACT

Background: The Coronavirus Disease 2019 (COVID-19) pandemic significantly impacted the older adult population globally. This study aimed to investigate cognitive function and its relationship with inflammation in older COVID-19 survivors over a three-month follow-up to address concerns about cognitive impairment and its risk factors.

Methods: In this descriptive-analytical study, 177 hospitalized COVID-19 patients aged >60 were assessed from July 2021 to February 2022. Psychiatric, global cognitive assessments and activities of daily living were conducted at discharge, 1 month, and 3 months post-discharge. Statistical analyses were conducted using SPSS Version 24. The evolution of cognitive status over time was evaluated using the Repeated Measures Test. The study probed into the association between inflammatory markers and cognitive function through the Pearson correlation test and the Mann–Whitney U test. Additionally, the link between anxiety/depression and cognitive performance was examined using the Pearson correlation.

Results: Results indicated that higher levels of C-reactive protein (CRP), D-dimer, and Lactate Dehydrogenase (LDH) were correlated to reduced cognitive performance. Conversely, Erythrocyte Sedimentation Rate (ESR) and Creatine Phosphokinase (CPK) did not exhibit a significant relationship with cognitive scores. A positive correlation was observed between improved cognitive function (reflected by higher GPCOG scores) and lower levels of anxiety and depression (indicated by lower scores on the Hospital Anxiety and Depression Scale). Over the study period, cognitive function and anxiety scores showed an upward trend, whereas symptoms of depression and challenges in daily activities remained consistent.

Conclusions: The study highlights the enduring effects and detrimental role of inflammation on overall cognitive abilities among older survivors of COVID-19. It underscores the urgent need for

specialized interventions and rehabilitative strategies to facilitate sustained cognitive recuperation among these individuals.

Keywords: COVID-19, Cognition, Depression, Biomarker, Aged

Coronavirus Disease 2019 and its Impact on the Cognition of Older Adults: Unraveling the Role of Inflammation

1 Introduction

The Coronavirus Disease 2019 (COVID-19) pandemic, caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), originated in China and rapidly spread worldwide [1]. While respiratory symptoms are the primary manifestation of COVID-19, approximately 35% of patients also experience neuropsychiatric symptoms, including depression, anxiety, and cognitive impairment [2, 3]. Cognitive impairment is a debilitating symptom that can persist into the recovery phase known as long COVID [4]. Both depressive symptoms and neurocognitive impairment were identified three months after COVID-19 infection [5]. It is worth noting that depression has an impact on neurocognitive functions, which may reflect the presence of common inflammatory triggers [6]. Although the exact mechanisms underlying the neuropsychiatric manifestations remain unclear, several neurotoxic mechanisms have been proposed, suggesting that COVID-19 affects the brain through multiple independent pathways [7].

Systemic inflammation and cytokine storms play significant roles in the clinical presentation of COVID-19 infection [8] and are risk factors for both the development and exacerbation of cognitive impairment [9]. Following infection, persistent molecular and functional changes in the brain are associated with systemic inflammation [10, 11]. COVID-19 may lead to prolonged inflammation, even after viral clearance, which may predict the persistence of depression and neurocognitive disorders [12, 13]. Inflammatory markers increase blood-brain barrier permeability, allowing

neurotoxic molecules to infiltrate the Central Nervous System (CNS) [14]. Inflammation can also induce structural damage, such as hippocampal atrophy [15].

Several inflammatory indices, including the Erythrocyte Sedimentation Rate (ESR), C-reactive protein (CRP), Lactate Dehydrogenase (LDH), Creatine Phosphokinase (CPK), and D-dimer, are elevated during COVID-19 infection. These markers are not only associated with disease severity but also predict worse outcomes [16-19]. COVID-19 severity and outcomes are more prominent in older patients, with the majority of deaths occurring among this age group [20]. Age-related immune imbalances contribute to the excessive release of proinflammatory cytokines, leading to a cytokine storm [21].

Older individuals, along with other age groups, are particularly susceptible to adverse outcomes following COVID-19 infection. Research has shown that advanced age is a significant risk factor for severe COVID-19 outcomes [20] and studies have emphasized the potential for cognitive decline in older adults [22, 23]. While studies have highlighted the impact of inflammation on cognitive function in older adults [24], few studies have investigated the link between cognitive function and inflammation in elderly individuals who have recovered from COVID-19 [25]. There is a pressing need for more extensive research to understand this connection fully, particularly across varied demographics and in different contexts such as in developing and low-income nations. The increasing number of older adults highlights the importance of conducting geriatric research. It is particularly noteworthy that, to date, no research in low- and middle-income countries, Iran included, has examined cognitive function and associated inflammatory markers in elderly COVID-19 survivors during their recovery period.

Regarding the evaluation of patients observed in the literature [4,6], we hypothesize that COVID-19 negatively affects the cognitive performance of older patients over time. Drawing from the existing literature that establishes connections between inflammatory markers and cognitive function [9,15], our hypothesis posits that elevated levels of inflammatory markers are correlated with cognitive

impairment. Based on the literature [3, 6, 39], we also expect group differences concerning the role of depression and anxiety in cognitive impairment over time.

The research evaluated the cognitive and psychological well-being of elderly COVID-19 patients at the time of hospital discharge, as well as one and three months afterward. It investigated the correlation between cognitive deficits and inflammatory indicators such as ESR, CRP, LDH, CPK, and D-dimer, with the goal of pinpointing potential factors contributing to cognitive decline in those who have recovered from COVID-19. Additionally, the study examined the impact of depression and anxiety on the cognitive abilities of these patients.

2 Methods

2.1 Study Design and Participants

This descriptive analytics study focused on older adult COVID-19 patients admitted to a hospital affiliated with Ahvaz Jundishapur University of Medical Sciences or Ahvaz Naft Grand Hospital from July 2021 to February 2022. Inclusion criteria encompassed individuals aged 60 years and older, capable of undergoing cognitive assessments, without diagnosed neurocognitive disorders or major psychiatric/neurological disorders, delirium, or use of psychotropic medications. Patients unwilling to undergo follow-up assessments were excluded. Of 383 COVID-19-positive older patients according to Real-Time Reverse Transcription-Polymerase Chain Reaction (RT–PCR), Out of 211 individuals who met the inclusion criteria, 177 patients were ultimately selected for the study, following the exclusion of those who did not fully complete the required study questionnaires.

2.2 Patient Evaluation

COVID-19 infection was confirmed based on clinical presentation combined with a positive RT-PCR result from a nasopharyngeal swab. Written informed consent was obtained from all the subjects. Demographic information was collected.

A semi-structured psychiatric interview, conducted by a dedicated psychiatrist, was employed to investigate the presence of any psychiatric disorders related to the inclusion and exclusion criteria based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). [26].

Prospectively, patients' mental and cognitive states were assessed at the time of hospital discharge and 1 month and 3 months post-discharge.

2.3 Psychiatric and Cognitive Assessment

Patients' mental states were evaluated using the Hospital Anxiety and Depression Scale (HADS) for anxiety and depression screening. The General Practitioner Assessment of Cognition (GPCOG) was employed for global cognitive evaluation. Basic Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) questionnaires were used to assess patients' functional status.

Hospital Anxiety and Depression Scale (HADS): The Hospital Anxiety and Depression Scale (HADS) is a widely used self-report questionnaire designed to assess and screen for symptoms of anxiety and depression in patients with physical health conditions [27]. It was specifically developed to address the challenges of identifying emotional distress in medical settings and is considered a reliable and efficient tool for this purpose. The HADS consists of two subscales, the HADS-Anxiety Scale (HADS-A) and the HADS-Depression Scale (HADS-D), each comprising seven items. Each item on the HADS is scored on a Likert scale, typically ranging from 0 to 3, with higher scores indicating greater symptom severity. The total score for each subscale (HADS-A and HADS-D) ranges from 0 to 21, with higher scores reflecting higher levels of anxiety or depression. The reliability of the HADS anxiety and depression subscales in the Iranian version has been reported with Cronbach's alpha coefficients of 0.85 and 0.70, respectively. In the Iranian adaptation of the HADS, the cutoff for diagnosing anxiety and depression is set at a score of 6. For depression, a score between 0 and 6 denotes the absence of depression, 7 to 8 suggests mild depression, 9 to 10 indicates moderate depression, and a score of 11 or higher signifies severe depression. In the case of anxiety,

a score from 0 to 6 implies no anxiety, 7 to 9 represents mild anxiety, 10 to 13 indicates moderate anxiety, and a score exceeding 14 points to severe anxiety [28].

General Practitioner Assessment of Cognition (GPCOG): The General Practitioner Assessment of Cognition (GPCOG) is a brief cognitive screening instrument designed for primary care settings, which aids general practitioners in identifying potential global cognitive impairment in older adults [29]. It has two components: a patient examination (GPCOG-P score: 0-9) and an informant questionnaire (GPCOG-I score: 0-6). The GPCOG - patient assesses four cognitive aspects, including orientation, recent information retrieval, executive function, visuospatial ability, and delayed recall . The GPCOG-informant interview comprises six questions covering cognitive and functional abilities concerning problems recalling recent events, misplacing objects, word-finding difficulties, managing finances, managing medications, and requiring help for transportation [30]. the Iranian version, Cronbach's alpha values for the GPCOG patient and informant subscales were 0.90 and 0.83, respectively, indicating high internal consistency and homogeneity between items. The test-retest correlation for the total P-GPCOG score was 0.82 in 30 participants after 19 days [31]. The utilization of the General Practitioner Assessment of Cognition (GPCOG) as a screening tool for dementia demonstrated its effectiveness in primary care settings. The comparison between GPCOG and the Mini-Mental State Examination (MMSE) revealed that both tools were similarly effective in detecting likely dementia. Moreover, the GPCOG was found to be a viable alternative to MMSE, requiring less time for administration while maintaining efficacy in screening for dementia [32]. Additionally, incorporating feedback from informants into the cognitive assessment procedure significantly improves the appraisal of cognitive health among older patients [33].

Basic Activities of Daily Living (BADL) and Instrumental Activities of Daily Living (IADL): The Basic Activity of Daily Living (ADL) is an assessment tool used to evaluate an individual's ability to independently perform basic self-care activities necessary for daily living and is commonly employed in older adults and individuals with disabilities. BADL typically comprises a set of fundamental activities, and individuals are evaluated based on their ability to perform these activities.

The BADL scale consists of 8 items, each scored from 0-2. Patients were categorized as independent (12-18), needing help (8-11), or dependent (0-7).

The IADL score assesses more complex activities that contribute to independent living. It includes managing finances, meal preparation, housekeeping, shopping, and medication management. It consists of 7 items, each scored using a scale (0-2). Accordingly, patients were considered independent (11-14), needed help (7-10), or dependent (0-6). The content validity index was greater than 0.82 for BADLs and IADLs in Persian. The sensitivity and specificity of the BADL and IADL were 0.75 and 0.96, respectively, and Cronbach's alpha was more than 0.75 [34].

2.4 Inflammatory Marker Assessment

Upon admission, a serum sample was obtained, and inflammatory marker (ESR, CRP, D-dimer, LDH, and CPK) levels were measured. CPK and LDH were analyzed by the HITACHI 902 instrument based on the instruction of the Bioinks Kit with lot no. 140805 for CPK and 141938 for LDH. Moreover, ESR was determined by using the automated ESR analysis instrument (Therma). CRP was evaluated based on the Unit kit using the BT3000 Autoanalyser instrument. According to the kit, CRP had a cut of that less than 6 has been considered as negative, and more than 6 was positive. This point was the same as D-dimer. So, we tested it using the Stago instrument, and the amount of more than 500 was considered positive, and less than 500 was negative.

2.5 Statistical analysis

Statistical Package for the Social Sciences (SPSS) Version 24 (IBM Corp., Armonk, N.Y., USA) was used for the statistical analyses. The normality of the data was checked using the Kolmogorov–Smirnov test. An alpha level of $P<0.05$ was considered to indicate statistical significance. Quantitative variables are presented as the mean and standard deviation. The Repeated Measures ANOVA and the Bonferroni post hoc test was used to compare the cognitive status, psychological function, BADL, and IADL of patients over time including at discharge, and 1 month and 3 months after discharge. The correlation between anxiety/depression and cognition was assessed using the Pearson correlation. Pearson correlation was used to investigate the associations between cognitive

function and parametric inflammatory indices. Quantitative variables of D-dimer and CRP were reported as Binary and Categorical (positive and negative), so the non-parametric Mann-Whitney test was used to compare the quantitative values between the two groups (Comparison of cognitive scores between two groups whose laboratory values were reported as positive or negative).

3 Results

The average age of the participants was 68±6.94 years. Our analysis includes a total number of 177 participants, with 94 males and 71 females. The demographic characteristics of the patients are summarized in Table 1. The samples were consistent at different measurement times.

Table 1. Demographic characteristics of patients at hospital discharge

Variable		N	%
Gender	Male	71	o.40
	Female	94	0.53
Marital status	Single & Widowed	124	70.05
	Married	53	29.9
Educational level	≤ High school Diploma	135	76.3
	>High school Diploma	42	23.7
Job	Employed	17	9.6
	Retired	160	90.4

The results of repeated measures analysis for the cognitive and psychiatric assessments are presented in Table 2.

Table 2. Results of Repeated Measures Analysis for Cognitive (GPCOG-P and GPCOG-I) and Psychological Assessment

Variables	Discharge time Mean (±SD)	After 1 month Mean (±SD)	After 3 months Mean (±SD)	P-value
GPCOG-P	4.84 (±2.42)	5.04 (±2.45)	5.24 (±2.62)	<0.001
GPCOG-I	2.30 (±2.62)	2.82 (±2.72)	2.99 (±2.69)	<0.001
Anxiety	12.97 (±4.41)	12.50 (±4.90)	11.53 (±4.62)	<0.001
Depression	6.70 (±4.43)	6.46 (±4.57)	6.23 (±4.50)	0.12
BADL	14.92 (±1.62)	14.97 (±1.40)	14.90 (±1.42)	0.805
IADL	12.62 (±2.35)	13.03 (±1.33)	13.35 (±1.23)	<0.001

A post hoc pairwise comparison using the Bonferroni correction showed a significant difference between the mean scores of the GPCOG-P at discharge and 1 and 3 months later. The mean GPCOG-P score increased over 3 months. There was a significant difference between the mean GPCOG-I score and IADL score at discharge and three months later. The GPCOG-I and IADL scores of the participants showed significant improvement after three months. Nonetheless, the analysis revealed no significant variation in the GPCOG-I scores between months 1 and 3, nor in the IADL scores across the same timeframe. For anxiety scores, there was a difference between the mean scores at the time of discharge and the third month and between the first and third months, but there was no significant difference between the mean anxiety scores at discharge and the first month. Overall, the mean anxiety scores of the participants decreased after three months. There was no significant difference in depression scores throughout the study. The mean scores for BADL remained relatively stable during the study. In summary, these results suggest that there are significant improvements in cognitive functioning (GPCOG-P and GPCOG-I scores), anxiety levels, and IADL over time ($p < 0.001$). However, there were no significant changes in depression or basic activities of daily living (Table 2).

Table 3 summarizes the correlations between LDH levels, the ESR, and CPK levels and the cognitive function of patients at hospital discharge (GPCOG-P_0, GPCOG-I_0), 1 month later (GPCOG-P_1, GPCOG-I_1), and 3 months later (GPCOG-P_3, GPCOG-I_3) according to Pearson correlation analysis.

The results indicate that LDH is significantly correlated with cognitive function scores and that higher LDH levels are associated with lower cognitive function. Moreover, the ESR and CPK did not significantly correlate with cognitive function.

Table 3. Correlation coefficients between inflammatory indices and cognitive function

Variables	LDH	ESR	CPK
GPCOG-P_0	-0.306**	-0.33	-0.102
GPCOG-I_0	-0.302**	+0.096	-0.128
GPCOG-P_1	-0.337**	+0.137	-0.32
GPCOG-I_1	-0.217**	-0.08	-0.221
GPCOG-P_3	-0.345**	+0.099	-0.32
GPCOG-I_3	-0.156*	-0.103	-0.212

Note. *: P-value<0.05, **: P value<0.01, 0: at the time of hospital discharge, 1: 1 month after discharge, 3: 3 months after discharge

A comparison of the mean cognitive indices according to CRP and D-dimer levels using Mann–Whitney U analysis also revealed that the cognitive score was significantly greater in patients with negative D-dimer and/or negative C-reactive protein (CRP) levels than in patients with positive D-dimer and/or CRP levels. The results are summarized in Table 4.

Table 4. Comparison of average cognitive assessment scores based on CRP and D-dimer levels

Variables	CRP			D-Dimer		
	Negative	Positive	P-value	Negative	Positive	P-value
GPCOG-P_0 (Mean ± SD)	6.63±2.35	3.61±1.55	<0.001	6.10±2.59	4.00±2.01	0.001
GPCOG-I_0	4.90±1.70	1.70±2.55	<0.001	4.5±2.17	2.29±2.82	<0.001
GPCOG-P_1	7.08±2.24	3.6±1.29	<0.001	6.47±2.5	4.18±1.97	<0.001
GPCOG-I_1	4.2±2.32	1.54±2.5	<0.001	3.84±2.53	2.2±2.78	0.007
GPCOG-P_3	7.51±2.25	3.66±1.44	<0.001	6.91±2.48	4.32±2.19	<0.001
GPCOG-I_3	3.99±2.34	1.47±2.49	<0.001	3.58±2.52	2.4±2.98	0.112

Note. 0: at the time of hospital discharge, 1: 1 month after discharge, 3: 3 months after discharge

Table 5 reveals the correlations between age, depression, anxiety, cognitive function, and functional ability. Age was positively correlated with depression and anxiety scores. Better cognitive function (higher scores on GPCOG) was correlated with less anxiety and less depression (lower scores on Hospital Anxiety and Depression Scale). Better cognitive function is associated with improved daily activities. Anxiety and depression are also correlated. These correlations remained relatively unchanged throughout the study (Supplementary table 1 and 2).

Table 5. Correlations between variables at the time of discharge

Variables	GPCOG-P	GPCOG-I	BADL	IADL	Anxiety	Depression	Age
GPCOG-P	1	+0.76**	+0.34**	-0.15	-0.66**	-0.749**	-0.3**
GPCOG-I		1	+0.15*	-0.12	-0.72**	-0.75**	-0.16*
BADL			1	+0.43**	-0.24**	-0.21**	-0.16**
IADL				1	-0.07	-0.08	-0.02
Anxiety					1	+0.82**	+0.2**
Depression						1	+0.25**
Age							1

Note. *: P value<0.05, **: P-value<0.01

4 Discussion

The present study aimed to investigate the relationship between inflammation and global cognition in older survivors of COVID-19 three months after discharge. A cognitive assessment of patients indicated lower mean scores on the informant subscales of the GPCOG at the time of discharge and the 1- and 3-month follow-up intervals (2.30 (±2.62), 2.82 (±2.72), 2.99 (±2.69) respectively) compared to mean scores of informant subscale GPCOG in the validation study performed on community-dwelling older adults in Iran (3.49 (±2.24)) [31]. These findings are consistent with those of other studies that reported cognitive decline after respiratory distress syndrome [35] and COVID-19 infection [36].

The study's findings revealed that despite lower scores on the informant subscale of the GPCOG over time, patients showed significant improvement in cognitive function, as assessed by the GPCOG-P and GPCOG-I. These findings suggest that older COVID-19 survivors may experience recovery in cognitive abilities over time, which may lead to promising results for the overall well-being and quality of life of COVID-19 survivors. This upward trajectory in cognitive performance after recovery highlights the promising prospects for cognitive rehabilitation and recuperation in those who have faced cognitive difficulties due to COVID-19.

The mean anxiety and depression scores of patients were higher than the cutoff points for the diagnosis of anxiety and depression. While anxiety scores demonstrated improvement over time, depression scores remained relatively unchanged. It should be noted that both anxiety and depression could have detrimental impacts on cognitive function. The lack of improvement in depression scores may indicate the durability of cognitive impairment, while an anxiety reduction may contribute to improving trends in cognition. This significant discovery underscores the importance of implementing focused interventions to address depression, which is essential for reducing its negative impact on cognitive functions and general well-being [37].

Additionally, IADL improved significantly over time. IADL refers to more complex daily tasks that require greater global cognitive functioning, such as managing finances or using technology. The

lower IADL scores suggest that COVID-19 survivors may experience difficulties performing these complex tasks, potentially due to cognitive impairments. An improvement in cognition results in an improvement in IADL. However, there were no significant changes in Basic Activities of Daily Living (BADL) over time.

Cognitive function was negatively correlated with age, aligning with prior research that identified an increased risk of cognitive decline in older individuals post-COVID-19 [38]. Enhanced cognitive performance, as measured by higher GPCOG scores, was found to inversely relate to anxiety and depression, which corresponded to lower scores on the Hospital Anxiety and Depression Scale. Literature has consistently shown a bidirectional link between emotional well-being and cognitive capacity, underscoring the significant role of emotion-cognition dynamics [39]. Moreover, cognitive deficits have been associated with psychiatric conditions like depression in COVID-19 survivors [3] with such psychopathologies contributing to diminished cognitive abilities [6].

Correlation analysis between inflammatory markers and global cognitive function scores revealed a significant correlation between higher LDH and lower cognitive function, while neither the ESR nor the CPK concentration was significantly correlated with cognition. LDH is an enzyme that is highly expressed in brain cells and plays an essential role in the glycolytic pathway. LDH is a general indicator of tissue damage, such as encephalitis and ischemic stroke, and is considered an inflammatory marker [40]. Elevated LDH levels are inversely correlated with respiratory function in patients with COVID-19 [41]. Moreover, a subtle yet notable correlation exists between the reduction in gray matter volume and elevated levels of LDH, underscoring the consequential influence of LDH on cognitive functions [42].

The correlations of CRP and D-dimer with cognitive function were also explored in this study. Positive CRP and D-dimer levels were significantly associated with consistently decreased cognitive function. These findings suggest a potential link between inflammation (CRP) blood clotting (D-dimer) and cognitive function.

CRP is a strong indicator of acute inflammation, and there is a reverse correlation between respiratory performance and CRP [41]. Elevated CRP is a risk factor for developing cognitive impairment and dementia [43], and an association between CRP and cognition was shown for COVID-19 survival [44].

In patients with COVID-19, D-dimer levels during the acute phase are associated with cognitive impairment [45]. An elevated D-dimer concentration in patients with COVID-19 is a risk factor for venous thromboembolism [46]. Cerebral microthrombi may explain the relationship between a positive D-dimer level and cognitive decline, which has been observed post-COVID-19 autopsy [47]. Additionally, pulmonary hypoperfusion due to thromboembolism in the presence of higher D-dimer concentrations may lead to hypoxia and cognitive impairment [25].

The limitations of this study warrant consideration. Firstly, the small sample size may affect the generalizability of the results. Future research with larger, more varied cohorts is needed to deepen our understanding of the link between inflammation and cognitive decline in older adults who have recovered from COVID-19. Secondly, the lack of a control group with another respiratory illness challenges the specificity of cognitive deficits to COVID-19. Thirdly, the observational design limits causal inferences; thus, longitudinal and experimental studies are necessary to clarify the temporal and causal dynamics between inflammation and cognitive health. Fourthly, cognition in older adults is influenced by numerous factors, making it difficult to isolate the effects of inflammation. Fifthly, the study only measured peripheral blood biomarkers at hospital admission, not accounting for changes over time; a longitudinal approach could yield a fuller picture of cognitive outcomes post-COVID-19. Sixth, the absence of a validated cognitive score cut-off in the Iranian context hinders the assessment precision. Seventh, the study did not examine gender differences, which could be influential. Lastly, the GPCOG, being a brief screening tool, necessitates further investigation to identify cognitive domains most vulnerable to impairment.

5 Conclusion

In conclusion, this research adds valuable insights to the existing knowledge on the interplay between inflammation and overall cognitive performance among older individuals who have recovered from COVID-19. The study indicates that over time, there is a general improvement in cognitive abilities, anxiety levels, and Instrumental Activities of Daily Living (IADL), whereas depression and the ability to perform basic daily tasks may continue to pose difficulties. Furthermore, these outcomes illuminate the intricate interconnections between inflammatory processes and cognitive health, proposing that various inflammatory indicators could influence cognitive results differently. The implications of these findings are significant for crafting specialized intervention and rehabilitation programs aimed at fostering cognitive recuperation and enhancing the quality of life for those who have survived COVID-19. Nonetheless, it is imperative to conduct additional research to further elucidate the fundamental processes and the enduring impact of inflammation on the cognitive well-being of this demographic.

Statement of Ethics

This study was approved by the Bioethics Committee of Ahvaz Jundishapur University of Medical Sciences (registration number: IR.AJUMS.REC.1400.244) and was conducted according to the principles of the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study.

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Credit authorship contribution statement

Shahrzad Mortazavi: Resources; Writing - original draft; and Writing - review & editing. Vahid Rashedi: Methodology, Project administration, Writing – review & editing. Bahman Cheraghian:

Methodology, Software, Investigation, Writing – review & editing. Fatemeh Pourshams: Resources, Data curation, Validation, Writing – review & editing. Saeid Saeidimehr: Resources, Data curation, Writing – review & editing. Bahram Dehghan: Resources, Validation, Writing – review & editing. Maryam Pourshams: Conceptualization; Data curation; Project administration; Resources; Supervision; Validation; Visualization; Writing - original draft; and Writing – review & editing.

Declarations of interest

None

Conflict of interest

None

Funding

Not applicable.

Data availability

The data supporting the findings of this study are available upon reasonable request from the corresponding author.

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Appendix A. Supplementary data

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Highlights:

1. Emerging evidence suggests a connection between inflammation and cognitive deterioration in COVID-19 patients.
2. Improved cognitive performance is associated with lower levels of anxiety and depression.
3. Patients demonstrated a progressive improvement in cognitive abilities over the course of time.

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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