Research Paper

Assessment of Cognitive Disorders and Depression in Patients with a History of COVID-19 in Babol, Iran, during 2022

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ABSTRACT

Aims COVID-19 threatens not only the physical health of individuals but also their mental health, particularly in terms of emotions and cognition. Understanding the neuropsychological sequelae of COVID-19 is essential for comprehensive knowledge of the disease and for developing appropriate treatment strategies for those infected. This study aimed to assess cognitive disorders and depression in patients with a history of COVID-19 in Babol, Iran, during 2022.

Materials & Methods This cross-sectional analytical study examined 270 patients with COVID-19, confirmed by a positive polymerase chain reaction test recorded at the Babol University of Medical Sciences Deputy of Health in 2022, who were randomly selected. The data collection tools included a demographic questionnaire, the Beck Depression Inventory-II (BDI-II), and the Montreal Cognitive Assessment (MoCA), which the patients completed. After collection, the data were analyzed using SPSS software (version 27), employing the Mann-Whitney U, Kruskal-Wallis, and Spearman's correlation tests at a significance level of less than 5%.

Finding The mean age of the patients was 49.40 ± 12.37 years, and 57% were female. The mean cognitive impairment score in patients was 26.28 ± 3.04, and the prevalence of cognitive impairment was 27.0%. Cognitive impairments showed a significant inverse correlation with age, duration of symptomatic illness, and education level ($P < 0.05$), and no significant relationship with patients' gender ($P > 0.05$). The mean depression score of the studied patients was 14.49 ± 7.71, which, according to the questionnaire's scoring method, indicated a mild level of depression in these patients. Patient depression had a significant direct statistical correlation with age, duration of symptomatic illness, and education level ($P < 0.05$) and no significant statistical relationship with the patients' gender ($P > 0.05$).

Conclusion Patients with COVID-19 had mild depressive symptoms and a 27% prevalence of cognitive impairment, while their mean cognitive impairment score remained within the normal range. Attention to the mental health of these patients is recommended to improve symptoms of depression and cognitive disorders.

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مقاله پژوهشی

بررسی اختلالات شناختی و افسردگی در بیماران با سابقه کووید- ۱۹ در طی سال ۱۴۰۱ در شهر بابل

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چکیده

اهداف: کووید-۱۹ نه تنها سلامت فیزیکی افراد را تهدید می‌کند، بلکه سلامت روانی افراد، به ویژه از نظر احساسات و شناخت را نیز تحت تاثیر قرار می‌دهد. آگاهی از عوارض عصبی کووید-۱۹ برای شناخت کامل این بیماری و داشتن استراتژی مناسب درمانی در مبتلایان به این ویروس ضروری به نظر می‌رسد. مطالعه حاضر با هدف کلی ارزیابی اختلالات شناختی و افسردگی در بیماران با سابقه کووید- ۱۹ در طی سال ۱۴۰۱در شهر بابل انجام شد.

مواد و روش‌ها: مطالعه حاضر از نوع مقطعی تحلیلی بوده که به بررسی ۲۷۰ نفر از بیماران مبتلا به کووید-۱۹ دارای تست مثبت PCR ثبت شده در معاونت بهداشتی دانشگاه علوم پزشکی بابل در سال ۱۴۰۱ که به صورت تصادفی انتخاب شده بودند، پرداخت. ابزار مورد استفاده در این مطالعه پرسشنامه اطلاعات دموگرافیک، پرسشنامه افسردگی بک ۲ و پرسشنامه ارزیابی شناختی مونترال بود که توسط بیماران مورد مطالعه تکمیل گردید. داده‌ها پس از جمع‌آوری با استفاده از نرم افزار SPSS نسخه ۲۷ و با استفاده از آزمون‌های من ویتنی یو، کروسکال والیس و همبستگی اسپیر من در سطح معنی‌داری کمتر از ۵ درصد مورد تجزیه و تحلیل قرار گرفت.

یافته‌ها: میانگین سنی بیماران مورد مطالعه ۱۲.۳۷±۴۹.۴۰ سال بوده و ۵۷ درصد ایشان زن بودند. میانگین نمره اختلالات شناختی بیماران مورد مطالعه ۳.۰۴±۲۶.۲۸و شیوع اختلال شناختی ۲۷.۰ درصد بود. اختلالات شناختی ارتباط آماری معنی‌دار و معکوس با سن، طول مدت علامت دار بودن بیمار، سطح تحصیلات داشته (۰/۰۵>P) و ارتباط آماری معنی‌داری با جنس بیماران نداشت (۰/۰۵<P). میانگین نمره افسردگی بیماران مورد مطالعه ۷.۷۱ ± ۱۴.۴۹ بود که با توجه به شیوه نمره‌دهی پرسشنامه، نشان دهنده سطح خفیف افسردگی در این بیماران بود. افسردگی بیماران مورد مطالعه ارتباط آماری معنی‌دار و مستقیم با سن، طول مدت علامت دار بودن بیمار و سطح تحصیلات داشته (۰/۰۵>P) و ارتباط آماری معنی‌داری با جنس بیماران نداشت (۰/۰۵<P).

نتیجه‌گیری: بیماران مبتلا به کووید-۱۹ دارای سطوح خفیف افسردگی و شیوع ۲۷ درصدی اختلال شناختی همراه با میانگین نمره اختلالات شناختی در محدوده طبیعی بودند. توجه به سلامت روان این بیماران برای بهبود علائم افسردگی و اختلالات شناختی پیشنهاد می‌گردد.

نویسنده مسئول:

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Introduction

In December 2019, an epidemic emerged in Wuhan, China, which attracted global attention and became known as COVID-19 [1]. This virus rapidly spread to other countries, turning into a worldwide pandemic [2]. The symptoms of COVID-19 infection were directly associated with patients' age and immune status [3]. The most common symptoms included fever, cough, and fatigue [4]. Although the virus was primarily identified as a respiratory syndrome, recent evidence indicates that, in addition to systemic respiratory manifestations, 36.4% of patients with COVID-19 also exhibit neurological symptoms, such as headache, impaired consciousness, and paresthesia, which are more frequently observed in severe cases compared to mild or moderate infections [5].

COVID-19 can affect all organs of the body, but the brain is among those organs most commonly impacted by long-term complications. Major neurological manifestations and long-COVID-related effects on the brain include reduced concentration and impaired thinking ability, headaches, sleep disturbances, orthostatic light-headedness, paresthesia, depression, anxiety, cognitive impairments, and memory disorders [6]. Anxiety is the most common mood disorder following COVID-19 infection, while depression ranks as the second most prevalent mood disorder in patients with long COVID. Approximately 22% of individuals hospitalized with COVID-19 reported depressive symptoms up to three months after infection. Overall, the incidence of depression after long COVID has been reported to be higher than that associated with other viral diseases, such as influenza [7]. The annual incidence of major depressive disorder in the general population is 1.59% (1.89% in women and 1.1% in men). The average age of onset is approximately 40 years, and about 50% of affected individuals develop the disorder between the ages of 20 and 50 [8]. Studies show that in COVID-19 patients, depressive symptoms typically appear 12 weeks after recovery and hospital discharge, with a prevalence of 30%–40% [9].

Moreover, previous studies have confirmed the neurotropic and neuron-invading properties of coronaviruses in humans. Cognitive disorders identified following COVID-19 infection include dementia, Alzheimer's disease, and delirium [10, 11]. From a pathobiological perspective, the virus may affect the cerebral cortex, infect the hypothalamus and brainstem, and cause neurobiological changes that range from fluctuations in consciousness—such as drowsiness, confusion, and delirium—to Alzheimer's disease, dementia, and even coma in COVID-19 patients [12, 13].

$$n = \frac{\left(z_{1-\frac{\alpha}{2}}\right)^2 (p(1-p))}{d^2} = \frac{(1/96)^2 \times 0/2626 \times 0/7374}{(0/2 \times 0/2626)^2} = 270$$

understanding of the disease and for developing appropriate therapeutic strategies for affected individuals. Despite reports of persistent symptoms in the chronic phase of COVID-19, concerns remain about potential cognitive consequences. However, limited data are available regarding the nature and prevalence of these outcomes in Iran. Therefore, the present study was conducted to assess cognitive impairments and depression in patients with a history of COVID-19 in Babol, Iran, in 2022.

Participants and Methods

This was an analytical cross-sectional study. The study population included patients with a history of COVID-19 who had a positive polymerase chain reaction (PCR) test registered at the Health Deputy of Babol University of Medical Sciences, Babol, Iran, and met the inclusion criteria. Participants were selected using random sampling. The inclusion criteria included being 18 to 65 years, providing informed written consent to participate in the study, having a positive PCR test, and having no prior history of depression or cognitive impairment based on patient self-report. The exclusion criteria included incomplete questionnaires (more than 20% missing responses).

The sample size was calculated using a similar study [14] and a prevalence rate of 26% ($P = 0.26$) at the 95% confidence level, resulting in a total of 270 participants.

The instruments used in this study included a demographic variables checklist, the Beck Depression Inventory-II (BDI-II), and the Montreal Cognitive Assessment (MoCA). The demographic checklist recorded age, gender, educational level, and duration of symptomatic illness. The MoCA, developed by Nasruddin et al., was used to assess mild cognitive impairment (MCI) [15]. This questionnaire comprises eight domains, evaluating short-term memory, temporal-spatial awareness, executive functions, attention, concentration, language, orientation, and time-place awareness. Scores ≥ 26 indicated normal cognitive function, while scores < 26 suggested mild cognitive impairment or Alzheimer's disease. The maximum score on the questionnaire was 30 [16]. In a study examining the psychometric properties of the MoCA in Parkinson's patients in Isfahan, Iran, Cronbach's alpha was 0.77, concurrent validity was 0.79, sensitivity was 0.85, and specificity was 0.90 [17]. According to the MoCA guidelines, educational level affects the final score; therefore, one point was added for participants with 12 years of education or less to adjust for the potential adverse effect of lower education on cognitive performance. The BDI-II consists of 21 multiple-choice questions and is a self-administered scale that can be completed in 5-10 minutes. The test consists of 21 questions on various symptoms, and participants are required to respond to each item on a four-point scale from 0 to 3. Two items address affective symptoms, 11 address cognitive symptoms, two address observable behaviors, five address somatic symptoms, and one addresses interpersonal symptoms. This scale categorizes depression from mild to severe, with total scores ranging from 0 to 63. Scores can be interpreted as

follows: 0–13: minimal or no depression; 14–19: mild depression; 20–28: moderate depression; 29–63: severe depression [18]. The psychometric properties of the BDI-II were validated by Mohammadhani et al. in 2007, and the questionnaire's validity and reliability have been confirmed with a Cronbach's alpha coefficient of 0.91 [18].

After obtaining approval from the Research Council of the Faculty of Medicine and the Ethics Committee of Gonabad University of Medical Sciences (IR.GMU.REC.1401.183), coordination was established with Babol University of Medical Sciences (Babol, Iran). The researcher obtained a list of patient names and contact numbers with a history of COVID-19 and positive PCR results registered in 2022 by referring to the Health Deputy and Comprehensive Health Service Centers in Babol, Iran. This list was randomly sorted using the RAND function in Excel. Selected individuals were contacted by phone to verify eligibility, and the study objectives and procedures were explained. For those willing to participate, an appointment was scheduled for an in-person completion of the questionnaire. The participants themselves completed the questionnaires or, if necessary, were interviewed by the researcher.

Collected data were entered into SPSS software (version 27) and analyzed. Descriptive statistics (mean and standard deviation) were used for quantitative variables, and frequencies were used for qualitative variables. Normality was assessed using the Kolmogorov–Smirnov test. For data analysis aligned with the specific objectives, the Mann–Whitney U test, the Kruskal–Wallis test, the Spearman correlation, and regression analysis were used. A P-value of < 0.05 was considered statistically significant.

Results

In this study, 270 patients with a history of COVID-19 and positive PCR test results were examined. The mean age of the patients was 49.40 ± 12.37 years. of these, 57% were female and 43% were male (Table 1). The mean MoCA score in patients with a history of COVID-19 was 26.28 ± 3.04, which, according to the questionnaire guidelines, was within the normal range for cognitive impairment.

Table 1. Demographic Information of Patients with a History of COVID-19 in Babol, Iran

Variable		No. (%) Mean ± SD
Gender	Male	116 (43)
	Female	154 (57)
Education	Below diploma	73 (27)
	Diploma and an associate degree	134 (49.6)
	Bachelor's degree	49 (18.2)
	Master's degree and above	14 (5.2)
Age		49.40 ± 12.37
Duration of symptomatic illness (days)		6.67 ± 2.15

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However, 27.0% of patients scored below 26 and were considered to have cognitive impairment (Table 2). The mean depression score based on the BDI-II was 14.49 ± 7.71, indicating a mild level of depression.

According to the questionnaire classification, 53.3% had no or minimal depression, 26.7% had mild depression, 14.8% had moderate depression, and 5.2% had severe depression (Table 2).

Table 2. Description of Depression and Cognitive Impairment Scores in Patients with a History of COVID-19 in Babol, Iran

Variable		No. (%) Mean ± SD
Beck Depression Inventory Score (BDI-II)		14.49 ± 7.71
Montreal Cognitive Assessment Score (MoCA)		26.28 ± 3.04
Depression status	None or minimal	144 (53.3)
	Mild	72 (26.7)
	Moderate	40 (14.8)
	Severe	14 (5.2)
Cognitive impairment status	No cognitive impairment	197 (73.0)
	Cognitive impairment	73 (27.0)

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Statistical analysis showed that depression was significantly positively correlated with age, duration of symptomatic disease, and educational level ($P < 0.05$) but was not significantly associated with gender ($P > 0.05$). Additionally, cognitive impairment had a significant inverse correlation with age, duration of symptomatic disease, and educational level ($P < 0.05$) and was not significantly associated with gender ($P > 0.05$) (Table 3).

Table 3. Association of Demographic Variables with Depression and Cognitive Impairment in Patients with a History of COVID-19

Variable		*P*-Value
Cognitive Impairment	Age	< 0.001*
	Duration of symptomatic illness (days)	< 0.001*
	Gender	< 0.163**

	Education level		< 0.001***
	Age		< 0.001*
Depression status	Duration of symptomatic illness (days)		< 0.001*
	Gender		0.259**
	Education level		< 0.001***

* Spearman, ** Mann-Whitney U, *** Kruskal-Wallis

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Logistic regression analysis showed that increasing age was significantly associated with a higher likelihood of cognitive impairment; each one-year increase in age increased the odds of cognitive impairment by 4.3% (odds ratio [OR] = 1.043; P = 0.041). Furthermore, the illness duration had a significant effect on cognitive impairment; each unit increase in disease duration increased the odds by 21.5% (OR = 1.215; P = 0.026). Compared to the reference group (diploma holders), individuals with a bachelor's degree had significantly lower odds of cognitive impairment (OR = 0.022; P < 0.001). Gender had no statistically significant effect on cognitive impairment (P = 0.752) (Table 4).

Table 4. Logistic Regression Model Results for Factors Associated with Cognitive Impairment in Patients with a History of COVID-19 in Babol, Iran (2022)

Variable		B	Odds Ratio	95% CI		*P*-Value
Age		0.042	1.043	1.002	1.085	0.041
Gender	Female	-	1.000	-	-	-
	Male	0.122	1.130	0.529	2.413	0.752
Education	Below diploma	-	1.000	-	-	-
	Diploma and Associate	-2.563	0.077	0.036	0.166	< 0.001
	Bachelor's	-3.831	0.022	0.005	0.101	< 0.001
	Master's and above	-21.509	0.000	0.000	-	0.998
Duration of Symptomatic Illness (days)		0.195	1.215	1.023	1.444	0.026

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In the linear regression model for determining factors related to depression scores, the duration of illness had the most significant impact on depression scores (P < 0.001); with longer disease duration, depression scores significantly increased. Additionally, individuals with a master's degree or higher had lower depression scores compared to the reference group (below diploma) (P = 0.006). Other education levels, gender, and age did not show a significant effect on depression scores (P > 0.05) (Table 5).

Discussion

Salicylic The results of the present study regarding

cognitive impairments showed that the mean MoCA score in patients with a history of COVID-19 was 26.28 ± 3.04, which, according to the questionnaire guidelines, was within the normal range for cognitive function. However, 27.0% of patients had scores below 26, indicating cognitive impairment. Consistent with these findings, Haddad et al. reported no statistically significant difference in MoCA scores between COVID-19 patients and healthy individuals [19]. Conversely, Wang et al. reported mild cognitive impairments in COVID-19 patients [20].

Table 5. Linear Regression Model Results for Factors Associated with Depression Scores in Patients with a History of COVID-19 in Babol, Iran (2022)

Variable		B	Beta	95% CI		*P*-Value
Age		0.003	0.004	-0.070	0.075	0.945
Gender	Female	-	-	-	-	-
	Male	-1.122	-0.072	-2.711	0.467	0.752
Education	Below diploma	-	-	-	-	-
	Diploma and Associate	-1.110	-0.072	-3.119	0.890	< 0.001
	Bachelor's	-2.194	-0.110	-4.680	−0.293	< 0.001
	Master's and above	-5.43	-0.156	-9.290	-1.576	0.998
Duration of symptomatic illness (days)		1.789	0.498	1.372	2.206	0.026

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The results of the present study regarding cognitive impairments showed that the mean MoCA score in patients with a history of COVID-19 was 26.28 ± 3.04, which, according to the questionnaire guidelines, was within the normal range for cognitive function. However, 27.0% of patients had scores below 26, indicating cognitive impairment. Consistent with these findings, Haddad et al. reported no statistically significant difference in MoCA scores between COVID-19 patients and healthy individuals [19]. Conversely, Wang et al. reported mild cognitive impairments in COVID-19 patients [20].

In the study by Hartung et al., approximately nine months after COVID-19 infection, 26% of patients exhibited moderate cognitive impairment and 1% severe cognitive impairment [21]. Considering that both studies used the MoCA questionnaire to assess cognitive function, and in the present study, while the mean cognitive score was normal, the prevalence of cognitive impairment was 27%, the results of the study above are roughly consistent with our findings. Nevertheless, this comparison should be interpreted

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with caution because, unlike Hartung et al., our study lacked precise information on patients' cognitive status prior to COVID-19, which constitutes a significant limitation.

In a meta-analysis, Seban et al. reported that 1 in 5 individuals showed cognitive impairment 12 weeks or more after a COVID-19 diagnosis [22]. Bertocchi et al. [23] highlighted the potential impact of prior COVID-19 infection on memory and attention deficits, findings that align with those of the present study.

Regarding the relationship between demographic variables and cognitive impairment, our statistical analyses indicated significant associations between cognitive impairment and age, duration of symptomatic disease, and education level, so that the average score of cognitive impairment in patients increased with increasing age and duration of symptoms, and was significantly higher in patients with higher education. Given that a higher MoCA score indicated less cognitive impairment, this study found that cognitive impairment was significantly higher in older patients, those with longer symptom duration, and those with lower education levels. However, no statistically significant association was observed between cognitive impairment and patient gender. Regarding the relationship between age and cognitive impairment, consistent with our results, Zhou et al. also reported an increase in the incidence of cognitive impairment with increasing age [24]. The results of a review study by Dehghani et al. showed that one-third to one-quarter of elderly people with COVID suffer from cognitive problems caused by delirium [25]. However, Haddad et al. reported no significant association between age and cognitive impairment [19]. Regarding the relationship between gender and cognitive impairment, consistent with our results, Haddad et al. [19] also reported no relationship between these variables. Regarding the relationship between cognitive impairment and the duration of symptoms, previous studies have reported that cognitive impairment severity in patients with this virus depends mainly on the duration of hypoxia, which is also more common in severe disease [26]. On the other hand, the results of the studies by Haddad et al. [19] and Graham et al. [27] were inconsistent with our findings, and no relationship was reported between these two variables. However, regarding this difference in results, it should be noted that in both studies, only patients treated as outpatients were examined. Therefore, the difference in the results is not far from expected.

Regarding depression, our study showed that the mean BDI-II score in patients with a history of COVID-19 was 14.49 ± 7.71, indicating mild depression. Moreover, 46.7% of participants experienced varying degrees of depression. In contrast, in a 2011 study by Salmelian et al., the mean depression score among women attending health centers in Babol, Iran, was 6.5 ± 8.2 [28]. The comparison suggests that the average depression score increased significantly after the COVID-19 outbreak. Asghari et al. reported a mean depression score of 19.6 ± 8.11 among students at Babol University of Medical Sciences, Babol, Iran [29],

higher than the present study, likely due to pre-pandemic academic-related stress. Consistent with our findings, Balouch et al. [30], Bagheri and Fathi [31], and Khazaei et al. [32] reported mild depression in COVID-19 patients. Conversely, Shah et al. reported that most patients were in a normal state in terms of depression and did not have any characteristics of depression [33]. Studies in China reported higher rates of severe depression among COVID-19 patients [34-36]. A national study in Iran by Zolghadr et al. reported relatively high post-pandemic depression [37]. The differences between these studies' results and our findings may be due to differences in the study populations, the time periods, and the seriousness with which quarantine guidelines were implemented.

Regarding the relationship between demographic variables and depression, our statistical analyses indicated significant associations between depression and age, duration of symptomatic disease, and education level, such that the mean depression score increased with age and longer duration of illness, and was significantly higher among individuals with lower education levels. No significant association was found between depression and gender.

Similar to our findings, several studies, including Serbozi et al. [38], Namazinia et al. [39], Maroufizadeh et al. [40], Shah et al. [33], Huang and Zhao [34], and Heydranlou et al. [41], reported a significant association between age and depression in COVID-19 patients. However, other studies, including Balouch et al. [30], Soleimani Moghaddam and Balouchi [42], and Akbarpour et al. [38], found no significant relationship. It seems that as people age, have less energy, and lead busier lives, their social connections decrease. Also, with increasing age, physical problems increase, which are reciprocally related to psychological problems, and this can justify the association between age and depression. Regarding the relationship between gender and depression in patients with COVID-19, the results of the studies of Ansari et al. [43], Sarboozi et al. [38], Huang and Zhao [34], Heydaranloo et al. [41], and Soleimani Moghadam and Balochi [42] were consistent with the results of our study. They did not observe a statistically significant relationship between these two variables. In the study of Balouch et al., depression was significantly higher in men with COVID-19 than in women [30]. On the other hand, Maroufizadeh et al. [40], Wang et al. [36], Zhou et al. [44], Shah et al. [33], and Akbarpour et al. [45] reported a higher probability of depression in women with COVID-19 than in men. The composition of the patients studied in terms of gender and differences in the culture prevailing in the studied societies could be important factors in the differences in the results obtained. Another crucial finding of our study was a significant increase in depression scores following an increase in the duration of the patient's symptoms. In this regard, Shahbazi and Daneshnejad also mentioned this issue in their study and stated that depression was significantly higher in hospitalized patients than in outpatients [46]. Consistent with our results, Sood et al. [47] and Yang et al. [48]

also pointed out an increase in the probability of depression with a longer disease duration.

According to the available evidence regarding cognitive impairment and depression after COVID-19 infection, studies with larger samples and comprehensive neurological and psychiatric assessments are needed to ensure the relationship between these complications and neurophysiological, neurobiological, and psychological bases. One of the limitations of this study was the use of self-report questionnaires and the patients' self-declaration of having no history of depression or cognitive impairment, which may have caused a bias in the response. Also, the psychological state of the research units when answering the questionnaire could have affected their responses.

Conclusions

In this study, cognitive impairment in patients with COVID-19 had a prevalence of 27% according to the Montreal Cognitive Assessment; however, patients' mean scores were within the normal range. Additionally, approximately 50% of patients exhibited varying degrees of depression. Age, lower educational level, and longer duration of symptomatic illness were identified as risk factors for cognitive impairment and depression in these patients. According to the results of this study, it is essential to pay attention to the psychological issues and complications of patients with COVID-19, in addition to physical complications, especially in patients at risk, to improve the mental health of patients with this disease. Therefore, periodic visits by psychiatrists and clinical psychologists are recommended for patients with COVID-19 to prevent depression and cognitive disorders.

Ethical Considerations
Compliant with ethical guidelines

In the present study, the informed consent form and research checklist were approved by the Research and Technology Deputy of Gonabad University of Medical Sciences, Gonabad, Iran, with the ethics code IR.GMU.REC.1401.183, as part of a medical student thesis.

Authors' contributions

Study design: Elahe Nayeri Ahangar, Payam Saadat, Alemeh Doostdar; Data collection: Elahe Nayeri Ahangar, Payam Saadat; Data analysis: Elahe Rahimi; Manuscript writing: Elahe Nayeri Ahangar, Payam Saadat, Alemeh Doostdar, Elahe Rahimi; Reading and approval of the final draft: All authors

Conflicts of interest

The authors declared no conflicts of interest.

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