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CONSEQUENCES OF THE CORONAVIRUS INFECTION: THE POST-COVID SYNDROME AND MENTAL MANIFESTATIONS. LITERATURE REVIEW

Indira K. Zhumabekova[1*], https://orcid.org/0000-0001-9285-887X
Vilen B. Molotov-Luchanskiy[2], https://orcid.org/0000-0001-8473-4375
Larisa L. Macievskaya[2]

[1] NCJSC «Astana Medical University», Astana, Republic of Kazakhstan;
[2] NCJSC «Karaganda Medical University», Karaganda, Republic of Kazakhstan.

Abstract

Introduction. The pathogenetic aspects of the inflammatory syndrome and complications after coronavirus infection have different development mechanisms. Patients who have had COVID-19, after recovery, experience fatigue, shortness of breath, central nervous system dysfunction and other extrapulmonary symptoms. The article describes the features of the course of various clinical disorders after suffering from COVID-19. In addition, some mechanisms for the development of long-term consequences are discussed.

Aim. Conduct an analysis of the literature data on the pathogenesis, clinical manifestations and development of various manifestations of post-Covid syndrome, including cognitive impairment.

Search strategy: Full-text publications in English and Russian that are devoted to the problem of COVID-19 were included in this review. The search for sources was carried out in the following databases: PubMed, The Cochrane Library, Scopus, Elsevier, and E-library; by keywords, (COVID-19, coronavirus infection, SARS-CoV-2, post-acute Covid syndrome, cognitive impairment) from 2019 to 2022. According to the topic of study, 712 publications have been reviewed, 81 of which met the selection criteria and were included in this review.

Results. Numerous publications show that the range of clinical symptoms of post-Covid syndrome is wide. Research has identified the following mental consequences after a coronavirus infection: anxiety, memory and attention impairment, depression smell disorder, insomnia, debuts of known mental disorders. The global medical community has been introduced the concept of "long Covid", which combines subacute COVID-19 and post-Covid syndrome. Thus, a more detailed study of this problem is relevant with the search for algorithms for providing effective medical care for coronavirus infection and post-COVID disorders.

Key-words: *COVID-19, coronavirus infection, SARS-CoV-2, post-acute COVID syndrome, cognitive impairment.*

Резюме

ПОСЛЕДСТВИЯ ПЕРЕНЕСЕННОЙ КОРОНАВИРУСНОЙ ИНФЕКЦИИ: ПОСТКОВИДНЫЙ СИНДРОМ И ЕГО МЕНТАЛЬНЫЕ ПРОЯВЛЕНИЯ. ОБЗОР ЛИТЕРАТУРЫ

Индира К. Жумабекова*[1], https://orcid.org/0000-0001-9285-887X
Вилен Б.Молотов-Лучанский[2], https://orcid.org/0000-0001-8473-4375
Лариса Л. Мациевская[2]

[1] НАО «Медицинский университет Астана», г. Астана, Республика Казакстан;
[2] НАО «Медицинский университет Караганды», г. Караганда, Республика Казахстан.

Введение. Патогенетические аспекты воспалительного синдрома и осложнений после коронавирусной инфекции имеют различные механизмы развития. Пациенты, перенесшие COVID-19, после выздоровления сталкиваются с наличием усталости, одышки, нарушением деятельности ЦНС и другими внелегочными симптомами. В статье описываются особенности течения разных клинических нарушений, после перенесенного COVID-19. Кроме того, обсуждаются некоторые механизмы развития долгосрочных последствий.

Цель. Провести анализ данных литературы по вопросам патогенеза, клинических проявлений и развития различных проявлений постковидного синдрома, в том числе когнитивных нарушений.

Стратегия поиска: В исследовании изучены полнотекстовые публикации на английском и русском языках, которые посвящены проблеме COVID-19. Поиск источников проводился в базах данных: PubMed, The Cochrane Library, Scopus, Elsiever, Elibrary; по ключевым словам, (COVID-19, коронавирусная инфекция, SARS-CoV-2, постковидный синдром, когнитивные нарушения) с 2019 года по 2022 год. По данной теме выявлено 712 публикаций, 81 из которых соответствовали критериям отбора и были включены в этот обзор.

Результаты. Многочисленные публикации показывают, что спектр клинических симптомов постковидного синдрома широк. Исследованиями выявлены такие ментальные последствия после перенесенной коронавирусной инфекции, как: тревога, ухудшение памяти и внимания, подавленность, расстройство обоняния, инсомния, дебюты известных психических расстройств. Мировым медицинским сообществом введено понятие “длительный ковид”, который объединяет подострый COVID-19 и постковидный синдром. Таким образом, актуально более детальное изучение данной проблемы с поиском алгоритмов оказания эффективной медицинской помощи при коронавирусной инфекции и постковидных расстройствах.

Ключевые слова: *COVID-19, коронавирусная инфекция, SARS-CoV-2, постковидный синдром, когнитивные нарушения.*

Түйіндеме

КОРОНАВИРУСТЫҚ ИНФЕКЦИЯНЫҢ САЛДАРЫ: КОВИДТАН КЕЙІНГІ СИНДРОМЫ ЖӘНЕ ОНЫҢ ПСИХИКАЛЫҚ КӨРІНІСТЕРІ. ӘДЕБИЕТТІК ШОЛУ.

Индира К. Жумабекова*[1], https://orcid.org/0000-0001-9285-887X
Вилен Б.Молотов-Лучанский[2], https://orcid.org/0000-0001-8473-4375
Лариса Л. Мациевская[2]

[1] «Астана медицина университеті» КеАҚ, Астана қ., Қазақстан Республикасы;
[2] «Қарағанды медицина университеті» КеАҚ, Қарағанды қ., Қазақстан Республикасы.

Кіріспе. Коронавирустық инфекциядан кейінгі асқынулар мен қабыну синдромының патогенетикалық аспектілері даму механизмдері әртүрлі болып келеді. COVID-19-мен ауырған науқастар толық емделгеннен кейін әлсіздік, ентігу, орталық жүйке жүйесінің дисфункциясы және басқада өкпе ауруларынан тыс белгілерді сезінеді. Мақалада COVID-19-дан ауырғаннан кейінгі әртүрлі клиникалық бұзылулар ағымының ерекшеліктері сипатталған. Сонымен қатар, кейбір ұзақ мерзімді асқынулардың даму себептері талқыланады.

Зерттеудің мақсаты. Ковидтен кейінгі синдромының әртүрлі клиникалық көріністерін, олардың дамуы мен патогенезіне, сонымен қатар когнитивті бұзылыстар жайлы әдебиет деректеріне талдау жасау.

Іздеу стратегиясы: COVID-19 мәселесіне арналған ағылшын және орыс тілдеріндегі толық мәтінді басылымдарға зерттеу жүргізілді. Әдебиетті шолу 2019 жылдан 2022 жылға дейін арнайы кілт сөздерімен (COVID-19, коронавирустық инфекция, SARS-CoV-2, ковидтен кейінгі синдром, когнитивті бұзылулар) PubMed, the Cochrane Library, Scopus, Elsiever, Ellibrary мәліметтер базасында жүргізілді. Зерттеуге сай 712 басылым анықталды, олардың 81-і іріктеу критерийлеріне сәйкес келді және осы шолуға енгізілді.

Нәтижелер мен қорытындылар. Көптеген зерттеу жұмыстары ковидтен кейінгі синдромының клиникалық симптомдарының ауқымының кең екенін көрсетеді. Зерттеулер коронавирустық инфекциядан кейінгі келесі психикалық асқынуларды анықтады: мазасыздық, есте сақтау мен зейіннің нашарлауы, депрессия, иіс сезудің бұзылуы, ұйқысыздық, белгілі психикалық бұзылулардың дебюті. Сонымен қатар дүниежүзілік медициналық қауымдастық жеделдеу COVID-19 ағымы мен ковидтен кейінгі синдромды біріктіретін "ұзақ ковид" жаңа ұғымын енгізді. Сонымен, коронавирустық инфекцияға және ковидтен кейінгі асқынуларға тиімді медициналық көмек көрсету алгоритмдерін іздеу арқылы осы мәселені толығымен зерттеу өзекті жұмыс болып табылады.

Түйін сөздер: COVID-19, коронавирустық инфекция, SARS-CoV-2, ковидтен кейінгі синдром, когнитивті бұзылулар.

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Introduction

The world is currently facing a global challenge in the form of a novel coronavirus infection (COVID-19) [41]. At the end of December 2019, a widespread new coronavirus was announced, it was first detected in Wuhan city, People's Republic of China [13]. In January 2020, the coronavirus infection rapidly spread in the countries of Eurasia and America. The spread of this virus around the world makes us think about the threat of coronavirus infection to the population of the whole world. On February 11, 2020, WHO (World Health Organization) declared about the official name of new disease - COVID-19 (Corona Virus Disease). On March 11, 2020, the WHO issued a statement about COVID-19 as a pandemic. COVID-19 is an ongoing global health emergency caused by the SARS-CoV-2 virus. The total number of registered cases of the disease was more than 662 million, and the number of deaths was 7.51 million. According to several studies, the incubation period of COVID-19 could vary from 2 up to 9 and 14 days [6, 29, 40].

The novel coronavirus SARS-CoV-2 is a single-stranded RNA virus belonging to the Coronaviridae family, subgenus Sarbecovirus, genus Betacoronavirus. Coronaviridae (CoV) is a family of one of the main human pathogens with a wide tissue tropism.

The post-COVID-19 condition (post-Covid syndrome) is characterized by symptoms that develop after a coronavirus infection lasting more than 12 weeks. There are variable, cyclical and diverse manifestations of post-Covid syndrome. Signs of post-Covid syndrome may include: neurological manifestations, cognitive impairment, namely: impaired attention and memory, disorder of executive processes, etc. as well as fatigue, shortness of breath, myalgia, chest pain and others. The article describes the features of the course of various clinical disorders after suffering from COVID-19. In addition, some mechanisms for the development of long-term consequences are discussed.

Aim: Conduct an analysis of the literature data on the pathogenesis, clinical manifestations and development of various manifestations of post-Covid syndrome, including cognitive impairment.

Search strategy: Full-text publications in English and Russian that are devoted to the problem of COVID-19 were included in this review. The search for sources was carried out in the following databases: PubMed, The Cochrane Library, Scopus, Elsevier, and E-library. *Inclusion criteria for the literature review:* This study included articles published in English that examined the pathogenesis of Covid-19, and the consequences of coronavirus infection in the form of dysfunctions of organs and body systems, including impaired cognitive function. The keywords included: "COVID-19", "coronavirus infection", "SARS-CoV-2", "post-acute Covid syndrome" and "cognitive impairment" from 2019 to 2022. *Exclusion criteria involved*: sources earlier than 2019, abstracts; not meeting the requirements of evidence-based medicine. According to the topic of study, 712 publications have been reviewed, 78 of which met the selection criteria and were included in this review.

Results and discussion

Pathogenetic aspects of the COVID-19

The structure of the new SARS-CoV-2 virus consists of a spherical shell particle represented by a single-stranded RNA associated with a nucleoprotein inside the capsid, which consists of a matrix protein [1, 30]. Of interest is the S-protein, represented by spike glycoprotein surrounded by the SARS-CoV-2 virion, they are responsible for the penetration of this virus into the host cell by molecules imitated. Transmembrane receptors respond to the action of molecules, one of them is the angiotensin-converting enzyme (ACE) 2 [39]. However, structural analysis (Cryo-Electron Microscopy) showed that the binding affinity of the S protein of the SARS-CoV-2 virus to ACE2 receptors is approximately 10–20 times higher than the protein of the SARS-CoVS virus [67, 73, 76]. Based on this, it is worth noting that the difference between SARS-CoV-2 is its high contagiousness compared to SARS-CoV, even though they are close to each other in terms of the structure of the genomic sequence. Perhaps this is the reason for the rapid spread of the virus and the scale of infection.

In previous studies of COVID-19 patients was demonstrated serious violations in system of blood aggregation. Besides was shown a high risk of emergence pathological arterial and also venous thrombotic events together with microangiopathy, contributing to endothelial cell damage. Some researchers showed interest in the study of molecular and cellular mechanisms of the development of COVID-19 processes [1, 17]. In this context seems to be an important such result as the appearance of neutrophil cell traps (nets) that has been described in patients with COVID-19. Elevated levels of neutrophil activation and the formation of neutrophil traps have been reported in patients hospitalized with COVID-19 and are associated with a higher risk of developing pathological thrombotic complications [32, 79]. The inflammatory process occurs in blood vessels, which causes a high risk of pathological vascular events, in particular, the risk of venous thromboembolism [49, 58, 67]. Hyperactivity of the blood clotting system is a common sign of severe COVID-19 [58]. Indeed, in many patients there were changes that are regarded as prothrombotic signs, including increasing of fibrin degradation products (D-dimer), elevated fibrinogen levels, and decreasing of antithrombin [20, 60]. Significantly elevated levels of neutrophil extracellular traps were found in the blood of patients hospitalized with COVID-19 compared to healthy controls [53, 81]. Especially high level was found in the subgroup of patients with a thrombotic event. Thrombotic changes can contribute to damage in the lungs, heart, kidneys, and other organs.

Patients with COVID-19 are known to have a significant inflammatory response that can lead to multiple organ failure. Discloses that SARS-CoV-2 enters human cells via ACE-2 receptors. Morphological disorders of neutrophil cells, immature granulocytes and atypical lymphocytes [15, 80] were found in the peripheral blood. Two relevant case reports report a mild leuko-erythroblastic pattern with moderate anisocytosis, sparse dacrocytes, and erythrocyte agglutination [34]. In addition, in COVID-19, SARS-CoV-2, by joining ACE 2, could increase the level of angiotensin II and decrease the level of angiotensin, which leads to excessive expression of oxidative stress. This, in turn, will increase inflammation and cause dysfunction of endothelial cells and red blood cells. Thus, the results of studies conducted by *Troyer E.A. et al*. [64] indicate the presence of abnormal RBCs and hyper segmented neutrophils in peripheral blood coinciding with hospitalization of patients

with COVID-19. Such anomalies may be associated with cytokine storm and hyperinflation and overexpression of oxidative stress [26]. SARS-CoV-2 infection leads to acute lung lesion; edema, fibrinous or proteinaceous exudate, presence of hyperplastic pneumocytes, punctate inflammation, multinucleated giant cells, and diffuse alveolar damage is observed in the lungs [8, 63, 77, 76].

A distinguishing feature between the SARS-CoV-2 virus, SARS-CoV and the influenza virus is the ability of long-term presence in hosts. Several studies have determined that patients with severe COVID-19 had lymphopenia, impaired adaptive immunity, and uncontrolled congenital inflammatory responses [26]. It is noted that T-cells play one of the key roles in SARS-CoV-2 infection. Inflammatory response persists in patients who have not activated T-cell immunity [3, 33]. Cytokines, being key mediators in the pathogenesis of COVID-19, are known to have a profound effect on memory and attention. The SARS-CoV-2 virus binds to the angiotensin-converting enzyme 2 receptors (ACE2). Because of binding the virus to ACE2 receptors starts the internalization and provides the initiation of the replication cycle [47, 69]. Immunity during viral infections is realized through the cellular component. It is immune cells that are in the main direction of viral aggression during viral attacks. They detect foreign RNA and trigger processes that, in a general pathological sense, are inflammatory. Often these processes acquire a systemic character, scale up at the level of the body and, as a result, perform a barrier role, delaying the spread of viral infection. In study conducted by *Ye Q. et al.* [75] in connection with the study of the behavior of SARS-CoV-2, it was shown that the interaction of immunocompetent cells and the RNA of the virus triggers a positive feedback. That is, with an increase in the number of viruses and, accordingly, their contact with the cellular component of human immunity, the number of signaling molecules to which inflammatory cytokines respond also increases. Inflammatory processes triggered by cytokines, on the one hand, can interrupt the reproduction of the virus, but, on the other hand, can provoke the development of a cytokine storm.

Thus, instead of a reliable stabilization of protection against the virus, we get an uncontrolled increase in circulating inflammatory cytokines. A special clinical consequence of the coronavirus attack is an increase in the amount of interleukin-6 (IL-6), tumor necrosis factor-α (TNFa) and interleukin-1β (IL-1β) - key pro-inflammatory cytokines [46, 75]. As follows, these observations have generated a great number of publications about the neurological and psychiatric consequences of SARS-CoV-2 infection [16, 24, 68]. For example, one of the most widely cited studies on the neurological manifestations of COVID-19 united the prevalence of drowsiness with delusions, reporting them together as "cognitive impairment." Some authors noted elevation of the inflammation (C-reactive protein (CRP) or IL-6) is accompanied by cognitive impairment [22, 45, 78]. Potentiation of the pathological process is ensured by the penetration of the blood-brain barrier by the key cytokines IL-6 and TNFα. Microglia respond extremely quickly to this penetration. Its cells actively release interleukin-1β. Thus, the hippocampus is involved in the pathological circle, since interleukin-1β receptors are concentrated mainly in the postsynaptic areas of its neurons.

This sensitivity of the hippocampus to IL-1β and its involvement in the pathological process causes the clinical manifestation of memory impairment. It has also been established that there is another mechanism of action of the SARS-CoV-2 coronavirus on the brain. This mechanism is mediated through the known interaction of the virus with the ACE-2 receptor. Thanks to this linkage, the virus reduces the activity of BDNF (brain-derived neurotrophic factor). A number of cognitive impairments may be caused by ACE-2 inhibition and a decrease in BDNF levels [28].

Summarizing the described research results, we can talk about the concept of direct involvement of the central nervous system in pathological processes during coronavirus infection, formed in these observations. The brain of a person suffering from COVID-19 or having had this infection is exposed to a threat from pro-inflammatory cytokines, primarily IL-6, which easily cross the blood-brain barrier (BBB). Microglia respond to IL-6 penetration. As well as other cytokines by their activation. Astrocytes produce an inflammatory signal that quickly spreads throughout the neural network. Hence, both severe neurological symptoms at the height of coronavirus disease and severe consequences for memory and cognitive functions in the long term after an apparent complete recovery.

Consequences of coronavirus infection

This poses the question if COVID-19 cause long-term consequences. Moreover, in a recent study conducted by a group of American scientists (*Tenforde M.W. et al.)* [61] in 2020, involving 120 patients who recovered from COVID-19, common symptoms were noted, such as shortness of breath (42%), memory loss (34%), sleep disturbances (30.8%) and difficulty concentrating (28%). After recovery, patients complained of myalgia, severe fatigue, feeling feverish, shortness of breath, chest tightness, tachycardia, headaches, and restlessness.

Carfi A. et al. [5] in their studies of 70% of the respondents had symptoms such as shortness of breath, chest tightness, fatigue, chills or sweating, body aches, dry cough, fever, headache, "brain fog" and concentrating problems [7]. Long-term endocrine and metabolic complications of COVID-19 include an increased risk of hyperglycemia, dyslipidemia, hypocorticism, and primary or central hypothyroidism. Psychiatric manifestations of COVID-19 have been associated with varying degrees of depression, sleep disturbance, and anxiety.

COVID-19 infection leads to long-term effects. In a recent study conducted by a group of scientists (Huang C. et al.) showed that 75% of people hospitalized with coronavirus infection experience post-acute COVID symptoms within 6 months after recovery, including fatigue, muscle weakness, depression, and sleep disturbance [25].

The SARS-CoV-2 virus causes toxic encephalopathy due to severe hypoxia. Nearly 40% of COVID-19 patients have cerebral symptoms. Similar complications of reversible brain dysfunction syndrome have been described in previous years during acute respiratory infection [11, 52, 54]. There are cases of viral brainstem infiltration, which were detected in tissue samples at autopsy, which suggested a viral mechanism of respiratory failure that develops in some patients due to damage to the cells of the respiratory center in the medulla oblongata. Some patients have cognitive impairment. So, for example, in a study

conducted by *Román G.C., Spencer P.S. et al*. a change in consciousness was noted in 69% of patients, and confusion in 44.8% of patients. After discharge, 33% of patients continued to have impaired attention and disorientation [52].

According to some authors, ACE2 mRNA has been found in cells of the cerebral cortex, striatum, hypothalamus, and brainstem. The virus also has the function of neurotropism, in addition, it is able to spread to the central nervous system. When analyzing genomic sequences, it was found that SARS-CoV-2 is 82% identical to SARS-CoV. The pathological mechanism of invasion of the SARS-CoV-2 virus into the CNS is most likely similar to that of the SARS and MERS viruses. Some patients have post-covid migraine-like cephalalgia, which persists for more than 6 weeks [48]. Chronic fatigue syndrome, characterized by a protracted course, decreased exercise tolerance, and rapid fatigue, persists for six months after a coronavirus infection, which causes the production of pro-inflammatory cytokines, and autoantibodies against enzymes that regulate energy metabolism [5, 37]. Such complications of COVID-19 may occur in 30-50% of convalescents; and in patients who were in intensive care units, as well as with concomitant diseases, they are more pronounced [36, 74]. The remaining negative changes in physical and social functioning negatively affect the quality of life and subsequent rehabilitation of patients.

For acute disease period along with the frequently occurring respiratory syndrome, the proportion of which reaches 45-100%, the astheno-neurotic syndrome is observed, including fatigue, anxiety, irritability, memory impairment, dizziness, depression, as well as a disorder of smell, and taste. 31% of patients have insomnia, and 19% of them have taste perversion and smell disorder. [19, 35, 65] Post-COVID symptoms include debilitating fatigue, headaches, shortness of breath, joint and muscle pain, mood swings, fatigue, decreased exercise tolerance, and memory loss. These symptoms appear months later, in previously healthy people [7, 18, 56].

Cerebral vascular disease is a serious complication of severe coronavirus infection. Patients with COVID-19 are more likely to develop acute cardiovascular disease than those with SARS and MERS. Neurological complications such as stroke, ischemic brain damage, thromboembolic occlusion of cerebral vessels, which is a predictor of vascular dementia and cognitive impairment, have been identified [42, 43, 46].

Neurological disorders and cognitive disorders after coronavirus infection

According to the literature, the neurological consequences after COVID-19 may develop due to a combination of the following factors [23]. First of all, cerebral hypoxia, diffuse damage to the white matter due to cardiorespiratory disease; second, cerebral microvascular lesions and endothelial dysfunction; thirdly, dysfunction of the renin-angiotensin system [10, 62, 70]. These mechanisms may contribute to the development of long-term neurological consequences in patients who have experienced COVID-19 [31, 57].

Brain is particularly vulnerable to hypoxia because cognitive neural processes do not adapt well to hypoxic conditions. As viral load increases, cognitive impairment increases. Based on the relationship between nerve tissue and oxygen levels, mitochondrial dysfunction caused by SARS-CoV-2 infection may be the basis for the neurological consequences associated with COVID-19.

Key issue after suffering from COVID-19 is not only neurological consequences but also problems with mental and psychological status disorders. In the study *Rogers J.P., Chesney E., et al.* noted that manifestations of a disturbed psyche are manifested by cognitive, and somatic disorders, as well as the presence of depression (10-15%) and anxiety-phobic (from 9-25%) states [51]. The causes of these conditions can be distress syndrome, the development of complications, self-isolation, and staying in the intensive care unit. According to a systematic review conducted by a group of scientists (*Troyer E.A., Kohn J.N. et al.)* [64], neurological disorders are detected in 25% of patients and require medical attention. These include panic attacks, psychomotor agitation, confusion and impaired consciousness, disorientation, delirium, and epileptic seizures [2, 9, 49].

A study conducted through an online survey launched in September 2020 (*Hannah E. Davisa L. et al.*) found that 86.7% of respondents who had a coronavirus infection reported fatigue. An interesting fact is that 1,700 respondents (45.2%) were unable to work full time; they even stated the need to reduce working hours compared to the period before the disease. More than a fifth of respondents, namely 839 people (22.3%) were unable to work due to illness at the time of the survey. Cognitive problems and memory impairments have been reported in all age groups [21].

The SARS-CoV-2 virus can directly affect the brain, and there may be infectious and inflammatory mechanisms. In the study conducted by a group of scientists (*Shai Betteridge, Jessica E.*) 31% of patients had serious changes of mental status. From this subgroup encephalitis was detected in 18%, unspecified encephalopathy in 23% and neuropsychiatric disorder in 59% of patients. 23 cases classified as neuropsychiatric were reviewed. 43% from them were described as psychoses, 26% as neurocognitive disorders and 30% as other mental disorders. 5% of the total were classified as having a peripheral disorder and 2% of other neurological disorders [55].

Fan B.E., Lim K.G.E. et al., in their study, retrospectively assessed cognitive pattern in patients who had recovered from coronavirus infection and were undergoing rehabilitation. The results revealed subclinical changes that could be determined by analyzing records in medical records. The presumptive correlation between verbal memory impairments and inhibition of functions provided by centers in the frontal lobes of the brain requires, according to the authors, careful research.

An adequate objective assessment of the cognitive abilities of patients who have suffered coronavirus infection is necessary in order to assess both the degree of their degradation and the possibility of further improvement of their condition. For example, patients who recovered from SARS-CoV-2-associated pneumonia and underwent rehabilitation showed abnormalities on clinical neurological examination. They required extensive neuropsychological examination [14].

At the same time, other patients had various neuropsychic disorders associated with the infection. Thus,

in a group of 10 patients who recovered from COVID-19, six people had normal cognitive status before the disease. But they showed signs of frontal or dissection dysfunction. Two patients had pre-existing severe cognitive impairment and it worsened. Another two patients had difficulties with verbal memory. Thus, in this group of patients, all had adverse cognitive-behavioral consequences after coronavirus infection.

The study by *Pietro Davide Antonio Di et al* (2021) assessed clinical neuropsychological findings in patients with COVID-19. The following disorders were diagnosed: one patient had difficulties accessing vocabulary in a semantic sense, 2 patients had visual and spatial impairments, 4 patients had deficits in executive functions (reasoning, attention, switching), 2 patients had difficulties with verbal memory. Frontal behavioral signs (disinhibition) were observed in 2 patients. The final diagnosis was made based on the sum of scores on the MMSE and Milan Score scales. It included a basic definition and assessment of the cognitive domain, detailing disorganization of cognitive-behavioral skills. For example: mild cognitive impairment with deficits in divided attention, abstraction, deductive reasoning and constructive apraxia [44]. However, this study did not compare with a control group of patients who had no history of coronavirus infection. It should be noted that these diagnoses may also be associated with more serious neurological problems associated with coronavirus damage to both the central and peripheral nervous systems.

The authors of these studies point to socio-psychological problems that cause the consequences of COVID-19. Reduced ability to work due to cognitive dysfunction, in addition to other neuropsychiatric disorders, led the examined patients to loss of ability to work, work and disability, and significantly worsened the quality of life of a large part of the patients.

Patients with neurocognitive deficits complain of problems with daily activities, communication with others, assimilation of new information, and understanding and reproduction of information. When evaluating neuropsychological testing and motor activity, problems with attention, understanding, memorization and reproduction of several words, numbers, and figures are revealed. Adaptive behavior, cognitive activity, working capacity, comprehension, episodic, procedural, semantic, operational, fixative and short-term memory suffer [59, 70]. Mental and behavioral disorders are one of the characteristics of the post-Covid "tail" [12, 58]. The reason for their development may be an incomplete restoration of mental and physical health, fear of re-infection, and fear of possible complications. The main manifestations of mental disorders include asthenia, anxiety, post-traumatic stress disorder, phobia, panic attacks, anxiety disorder, and depression [49, 71]. A manifestation of emotional instability is irritability, tearfulness, and rapid mood swings. Complications such as encephalitis, ischemic stroke, intracerebral hemorrhage, psychosis or neurocognitive syndrome have also been reported [38, 50, 66].

According to the research results conducted in Italy by *De Lorenzo R., Conte C. et al*., among 185 patients verified COVID-19, 25% had cognitive impairment. The study included patients aged 18 years and older with no previous history of cognitive impairment [12]. According to some studies, the presence of symptoms such as headache (in 44% of cases), fatigue (58%), and impaired attention (27%) was revealed. Coronavirus infection harms the brain, disrupts its functioning, causes intoxication of the body, and an increase in the number of endotoxins, as a result, the functioning of the nervous system deteriorates, neurodegeneration and cognitive impairment occur [4, 72].

On the other hand, plenty of literature does not reflect information about already existing cases of cognitive impairment in patients with COVID-19, whether this disease was the cause of cognitive impairment.

It is also required to take into account the relationship between emotional state, levels of anxiety and depression, and cognitive functions. It is necessary to study the impact of cognitive impairment on daily life, and the physical and psychological components of quality of life over time. Baseline studies should be conducted that examine at least five cognitive domains: attention, memory, language, executive function, and visuospatial function. They must be measured using reliable, valid tools that monitor learning effects.

Screening patients during the course of the disease using simple and basic tests that assess verbal and frontal memory functions can help identify the degree and level of the functional disorders and can help define patients who may benefit from a full - fledged neuropsychological estimation and cognitive rehabilitation. However, follow-up studies on COVID-19 patients are needed to quantify the frequency and relative risks of psychiatric sequelae following infection.

Conclusion.

As a result of the literature review, numerous studies were identified that examined the consequences of COVID-19. The most common features of post-Covid syndrome are: fatigue, shortness of breath, memory impairment and impaired attention, sleep disturbance, myalgia. The exact cause of prolonged manifestations of coronavirus infection is not clear. It is necessary to determine the predictors and factors that determine the duration and variety of manifestations of the post-Covid syndrome. Additional observations and carefully designed studies are needed to identify risk factors, mechanisms for the development of long-term consequences, as well as specific and effective management tactics for such patients. This issue remains relevant and requires further study to prevent adverse consequences.

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Сведения об авторах:

1. **Жумабекова Индира Кайратовна,** ассистент кафедры реабилитологии и спортивной медицины. НАО «Медицинский университет Астана». ORCID ID: 0000-0001-9285-887X, e-mail: Indira.z@mail.ru

2. **Молотов-Лучанский Вилен Борисович,** доктор медицинских наук, профессор. НАО «Медицинский университет Караганды». ORCID ID: 0000-0001-8473-4375, e-mail: Molotov-luchanskiy@qmu.kz

3. **Мациевская Лариса Леонардовна,** Ассоциированный профессор Кафедры неврологии, психиатрии и реабилитологии. НАО «Медицинский университет Караганды». e-mail: Macievskaya@qmu.kz. г. Караганда, Казахстан.

***Corresponding author:**
Indira K. Zhumabekova, Assistant at the Department of Rehabilitation and Sports Medicine. NJSC "Astana Medical University", Astana, Republic of Kazakhstan.
Mailing Address: 010000, Kazakhstan, Astana city, Kazibek bi street 3.
E-mail: Indira.z@mail.ru
Phone number: +7 775 951 48 13