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**ANXIETY-DEPRESSIVE DISORDERS AFTER COVID-19**

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The 2019 coronavirus (COVID-19) pandemic has reached more than 194 million people as of July 26, 2021, and continues to spread worldwide. During the course of the long pandemic, evidence of damage to various organs and systems, such as the nervous system and parts of it, began to emerge. Oxidative stress is one of the main causes of neuronal dysfunction and death, mainly due to excessive formation of reactive oxygen species and depletion of antioxidant reserves. Oxidative stress is characterized by an imbalance between the production of reactive oxygen species (ROS) and antioxidant defense mechanisms of the body. This process is involved in the onset and development of many neurological diseases. In this review, we analyzed and summarized the results of studies showing the association of neurological diseases, such as stroke, Parkinson's disease, and other neurological diseases, with excessive formation of oxidative stress products. This article aims to provide an overview of the relationship between oxidative stress and a range of neurological conditions, shedding light on the underlying mechanisms and potential therapeutic implications. Objective of the study was to determine the level of anxiety-depressive disorders among patients who underwent COVID-19. 90 people were examined and selected according to inclusion and exclusion criteria. To assess higher nervous functions, we used the hospital scales HADS I, HADS II, Beck depression scale. To date, our study has not found a clear link between the virus in the body and anxiety-depressive manifestations in patients, which may suggest that the main cause of the disorders lies in the social aspects of the pandemic.

*Key words:* anxiety; depression; COVID-19; COMPASS 31; post covid syndrome

## INTRODUCTION

In 2019, an outbreak of a new infection, which will later be called COVID-19, occurred worldwide. The 2019 coronavirus (COVID-19) pandemic has reached more than 194 million people as of July 26, 2021, and continues to spread worldwide [16]. The respiratory organs are the main target, but there have also been extrapulmonary manifestations. During the course of the long pandemic, evidence of damage to various organs and systems, such as the nervous system and parts of it, began to emerge. Different studies have shown that after the end of the acute phase of COVID-19, symptoms may persist despite elimination of the virus from the body, even if the person was asymptomatic [2]. According to the National Institute for Health and Care Excellence, the number of patients with various complaints began to increase after COVID-19. These manifestations were called «post-COVID syndrome» or «long COVID», is a term used to describe a range of physical and psychological symptoms that persist long after the acute phase of a COVID-19 infection has passed. By the World Health Organization criteria's post COVID-19 condition is usually diagnosed by a healthcare provider at least 3 months after a patient falls ill with COVID-19. This 3-month period allows healthcare providers to rule out the usual recovery period from an acute illness. Sometimes this recovery period can be long, especially if someone is very sick. Symptoms differ between people, and between adults and children. Overall, the most common symptoms of post COVID-19 condition include: fatigue, shortness of breath or difficulty breathing, memory, concentration or sleep problems, persistent cough, chest pain, trouble speaking, muscle aches, loss of smell or taste, depression or anxiety, fever. People with post COVID-19 condition, also known as long COVID, may have difficulty functioning in everyday life. Their condition may affect their ability to perform daily activities such as work or household chores [15]. There is a high frequency of neuropsychiatric symptoms among COVID-19 survivors, suggesting that COVID-19 affects the central nervous system (CNS) (e.g., SARS-CoV-2 neurotropism, hyperinfarction, and hypercoagulability

after infection, especially in severe cases) [4]. Studies of past pandemics caused by respiratory viruses have shown that different types of neuropsychiatric symptoms can occur both during the acute viral infection and after the infection has occurred over different periods of time. According to data from the 18th and 19th centuries, such as influenza pandemics, it is known that there was an increased incidence of various neuropsychiatric symptoms such as insomnia, anxiety, depression, mania, psychosis, suicidality and delirium [5]. During the "Spanish" influenza pandemic in the early 20th century, an increase in the incidence of lethargic encephalitis (LE), an inflammatory disease of the CNS characterized by hypersomnolence, psychosis, catatonia and parkinsonism, was recorded [6, 7]. Against the background of the 2009 influenza (H1N1) pandemic and other coronavirus infections (SARS-CoV-1 epidemic in 2003, (MERS-CoV) in 2012.), neuropsychiatric sequelae such as: narcolepsy, seizures, encephalitis, encephalopathy, Guillain-Barré syndrome (GBS) and other neuromuscular and demyelinating processes have also been reported [8, 9, 10, 11]. Depression, anxiety, and trauma-related symptoms have been associated with CoV virus outbreaks, but it is not fully clear whether these are related to viral infection per se or to the body's immune response. Studies of healthcare workers during the SARS-CoV-1 epidemic, the MERS-CoV outbreak, and the current SARS-CoV-2 pandemic show that the frequency and severity of psychiatric symptoms are associated with proximity to CoV-infected patients [12]. According to the literature, psychological and neuropsychological problems (anxiety and depression, post-traumatic stress disorder, sleep problems and cognitive problems) after COVID-19, even in individuals without previously diagnosed psychiatric disorders. This is consistent with the results of two meta-analyses conducted among survivors of previous coronavirus epidemics [13, 14], which showed that one-third of patients experienced at least one psychological disorder (PTS). At least one psychological disorder (PTSD, depression, and anxiety) more than 6 months after discharge. The prevalence of mental health symptoms varies considerably across studies, which may be due to differences in the instruments used to measure these indicators, as well as differences between countries regarding the influence of cultural or spiritual beliefs on attempts to coping with the psychological consequences of coronavirus disease [17, 18].

**Objective of the study** was to determine the level of anxiety-depressive disorders among patients who underwent COVID-19.

## MATERIALS AND METHODS

Participants. 90 people were examined and selected according to inclusion and exclusion criteria. Inclusion criteria: age between 18 – 60 years; history of coronavirus infection in the remote period, confirmed by laboratory and clinical tests; presence of complaints, disorders of the nervous system; absence of severe concomitant chronic pathology. Exclusion criteria: acute period of coronavirus infection; presence of severe concomitant chronic pathology; absence of complaints for nervous system disorders.

Ethical approval. This study was approved by the Local Ethics Committee of Karaganda Medical University. Study participants were fully informed of the purpose of the study and signed an informed consent form.

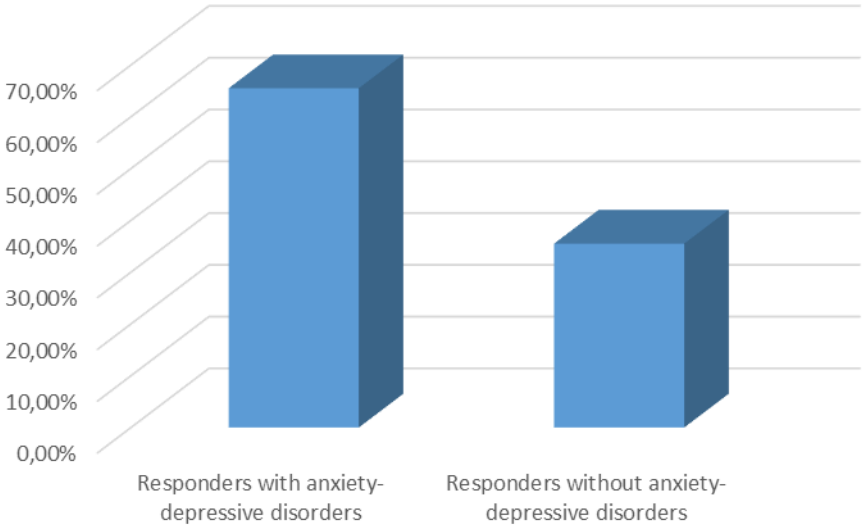


Figure 1 – Results of assessment of anxiety and depressive disorders among the patients

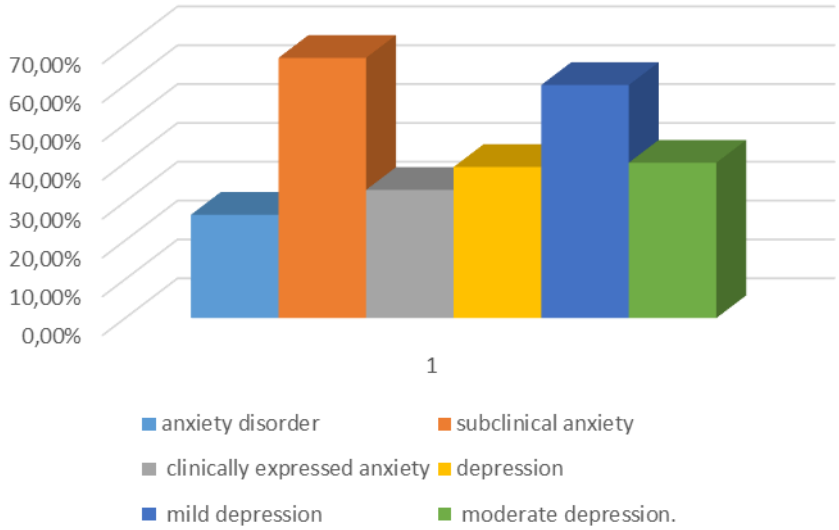


Figure 2 – Structure of anxiety and depressive disorders among the patients

Table 1 – Results of the Beck depression scale scores among the studied groups

| Group | Subclinical | Norm | Mild | Total |
|---|---|---|---|---|
| Control | 45 | 0 | 2 | 47 |
| Covid patients | 33 | 3 | 7 | 43 |
| Total | 78 | 3 | 9 | 90 |
| p-value = 0.02113 | | | | |

Table 2 – Results of anxiety level assessment on the HADS1 scale among the studied groups

| Group | Normal | Mild | Subclinical | Total |
|---|---|---|---|---|
| Control | 40 | 5 | 2 | 47 |
| Covid patients | 26 | 11 | 6 | 43 |
| Total | 66 | 16 | 8 | 90 |
| p-value = 0.02657 | | | | |

Table 3 – Results of anxiety level assessment on the HADS II scale among the studied groups

| Group | Normal | Mild | Subclinical | Total |
|---|---|---|---|---|
| Control | 37 | 9 | 1 | 47 |
| Covid patients | 30 | 9 | 4 | 43 |
| Total | 67 | 18 | 5 | 90 |
| p-value = 0.306 | | | | |

## RESULTS AND DISCUSSION

Among the patients studied, according to the history, 3.3% of patients had severe coronavirus infection, 23.3% of patients had moderate coronavirus infection and 42.2% had mild coronavirus infection, and 31.1% had no history of COVID (control group).

We investigated the functions of the higher nervous system. To assess higher nervous functions, we used the hospital scales HADS I, HADS II, Beck depression scale. Questioning of patients was carried out by means of paper and electronic media. Anxiety-depressive disorders developed in 65.5% of patients against the background of coronavirus infection (Fig. 1).

Among the patients of this group, 26.6% developed anxiety disorder, of which 67% had subclinical course and 33% had clinically expressed anxiety. Depression was detected among 38.9% of the patients in this group, 60% of them had mild depression; the remaining 40% had moderate depression (Fig. 2). The main complaints presented by patients are frequent mood changes, more often persistent lowering of emotional background, anxiety, fear, memory decline, poor concentration of attention. Patients note that these symptoms are most pronounced in the first months after the infection. However, even in the remote period, these complaints persist in varying intensity. The development of depressive-anxiety states is more characteristic of people who have had coronavirus infection with a more severe course. At the same time, patients with mild coronavirus infection are less susceptible to the development of depressive-anxiety states.

To determine the relationship between anxiety and depressive disorders in patients with a history of coronavirus infection, statistical analysis was performed using Fisher's criterion. According to the results of statistical data processing, no clear relationship between the results of Beck's scale, HADS and the history of coronavirus infection was found.

The results of Beck scale depression scores among the studied groups are presented in table 1.

The results of HADS1 anxiety scores among the study groups are presented in Table 2.

The results of anxiety level assessment on the HADS II scale among the studied groups are presented in Table 3.

Analysis of the results of comparison of clinical data and questionnaire indicators demonstrates dependence in all studied groups. Therefore, we can state the dependence of registered complications on the presence of coronavirus infection, but not on biochemical parameters.

## CONCLUSION

This the percentage of patients with anxiety-depressive disorder after COVID is not insignificant, as shown by these studies. However, this issue requires further and more in-depth study to determine a clear link between the trans-sensory infection and the development of the above-mentioned symptoms. To date, our study has not found a clear link between the virus in the body and anxiety-depressive manifestations in patients, which may suggest that the main cause of the disorders lies in the social aspects of the pandemic.

***Authors' contributions:***

Z. D. Kulbayeva – material collection and processing, text writing, statistical processing.

Sh. S. Kaliyeva – concept and design of the study.

D. A. Klyuyev – concept and statistical processing.

S. T. Tuleutayeva – editing.

***Conflict of interest.*** No conflicts of interest have been declared.

This material has not been previously submitted for publication in other publications and is not under consideration by other publishers. There was no third-party funding or medical representation in the conduct of this work.

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**ТРЕВОЖНО-ДЕПРЕССИВНЫЕ РАССТРОЙСТВА ПОСЛЕ COVID-19**

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Окислительный стресс является одной из основных причин дисфункции и гибели нейронов, главным образом из-за избыточного образования реактивных форм кислорода и истощения запасов антиоксидантов. Окислительный стресс характеризуется дисбалансом между производством реактивных форм кислорода (ROS) и антиоксидантными защитными механизмами организма. Этот процесс вовлечен в возникновение и развитие многих неврологических заболеваний. Авторы проанализировали и обобщили результаты исследований, показавших связь неврологических заболеваний, таких как инсульт, болезнь Паркинсона и другие неврологические заболевания, с избыточным образованием продуктов окислительного стресса, проанализировали взаимосвязи между окислительным стрессом и рядом неврологических заболеваний, оценили лежащие в их основе механизмы и потенциальные терапевтические последствия. Целью исследования было определение уровня тревожно-депрессивных расстройств среди пациентов, перенесших COVID-19. Были обследованы 90 человек, отобранных в соответствии с критериями включения и исключения. Для оценки высших нервных функций использовали госпитальные шкалы HADS I, HADS II, шкалу депрессии Бека. Проведенное исследование не выявило четкой связи между наличием вируса в организме и тревожно-депрессивными проявлениями у пациентов, что может свидетельствовать о том, что основная причина расстройств кроется в социальных аспектах пандемии.

*Ключевые слова:* тревога; депрессия; COVID-19; COMPASS 31; постковидный синдром

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**COVID-19-ДАН КЕЙІНГІ МАЗАСЫЗДЫҚ ПЕН ДЕПРЕССИЯЛЫҚ БҰЗЫЛУЛАРЫ**

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Тотығу стрессі нейрондық дисфункцияның және өлімнің негізгі себептерінің бірі болып табылады, негізінен реактивті оттегі түрлерінің артық түзілуіне және антиоксиданттық қорлардың азаюына байланысты. Тотығу стрессі реактивті оттегі түрлерін (ROS) өндірісі мен ағзаның антиоксиданттық қорғаныс механизмдері арасындағы теңгерімсіздікпен сипатталады. Бұл процесс көптеген неврологиялық аурулардың пайда болуына және дамуына қатысты. Бұл шолуда біз инсульт, Паркинсон ауруы және басқа неврологиялық аурулардың тотығу стресс өнімдерінің шамадан тыс қалыптасуымен байланысын көрсететін зерттеулердің нәтижелерін талдадық және қорытындыладық. Бұл мақаланың мақсаты - тотығу

стрессі мен бірқатар неврологиялық аурулар арасындағы байланысқа шолу жасау, олардың негізгі механизмдері мен ықтимал емдік салдарға жарық түсіру. COVID-19-дан кейінгі науқастардағы мазасыздық пен депрессиялық бұзылулардың деңгейін анықтау зерттеудің мақсаты болып табылған. Зерттеуге қосу және алып тастау критерийлеріне сәйкес 90 адам тексерілді. Жоғары жүйке функцияларын бағалау үшін ауруханаңың HADS I, HADS II, және Бек депрессия шкалалары қолданылды. Қорытындылар: бүгінгі күнге дейін біздің зерттеуімізде вирустың ағзада болуы мен пациенттердегі мазасыздық пен депрессиялық көріністер арасында нақты байланыс анықталған жоқ, бұл бұзылулардың негізгі себебі пандемияның әлеуметтік аспектілерінде жатқанын көрсетуі мүмкін.

*Кілт сөздер:* мазасыздық; депрессия; COVID-19; COMPASS 31; пост-ковид синдромы