

DIAGNOSTIC AND THERAPEUTIC ASPECTS OF POST-COVID CEREBRAL ASTHENIC SYNDROME

Shodiev Ulugbek Doniyor ugli

Candidate of Medical Sciences Tashkent State Medical University Tashkent, Uzbekistan

Abstract: The COVID-19 pandemic, which began at the end of 2019, not only drew attention to the acute manifestations of the infection but also revealed a wide range of long-term consequences united by the concept of "post-covid syndrome" or "long COVID." Among the multiple manifestations of this condition, a special place is occupied by the cerebral-asthenic syndrome, which is characterized by a complex of neurological and neuropsychiatric disorders that significantly reduce the quality of life of patients.

Key words: SARS-CoV-2, COVID-19, coronavirus, virus life cycle, pathogenesis, cytokine storm, ACE2 receptor, adhesive protein, immune response, inflammation, interleukins, virus replication, cell invasion, respiratory distress syndrome

Introduction. The pathogenesis of cerebral asthenic syndrome in COVID-19 is multifactorial and includes the direct neurotropic effects of SARS-CoV-2, systemic inflammation with microglia activation, impaired blood-brain barrier, hypoxic brain tissue damage, as well as the psychological consequences of severe illness[1].

Cerebroasthenic syndrome in the post-COVID period is a polyetiological condition that includes cognitive impairments ("brain fog"), chronic fatigue, emotional lability, sleep disturbances, headaches, and autonomic dysfunction. According to various studies, from 10% to 80% of patients who have had COVID-19 experience certain manifestations of post-COVID syndrome, while neurological symptoms are noted in 30-50% of patients and can persist from several months to a year or more [2]. Mitochondrial dysfunction and disruption of neuronal energy metabolism play a special role, which can explain the persistent nature of the symptoms.

Diagnosing cerebro-asthenic syndrome in the post-COVID period presents certain difficulties, as there are currently no unified diagnostic criteria and specific biomarkers. The clinical picture is often nonspecific and can overlap with other conditions, such as depression, anxiety disorders, or somatic diseases. This requires a comprehensive multidisciplinary approach using clinical scales, neuropsychological testing, and instrumental research methods [3]. Therapeutic approaches to treating cerebro-asthenic syndrome in the post-COVID period are being actively studied. Modern treatment strategies include symptomatic therapy, neuroprotective drugs, cognitive rehabilitation, physiotherapy methods, and psychological support. Special attention is paid to a personalized approach to treatment, taking into account the individual characteristics of the patient, the severity of the previous infection, and the prevailing clinical manifestations [4]. The relevance of studying cerebro-asthenic syndrome in the post-COVID period is due not only to its high prevalence but also to the significant socio-economic burden associated with decreased work capacity and quality of life of patients. Developing effective methods for diagnosing and treating this condition is a priority task of modern medicine and requires interdisciplinary collaboration between neurologists, psychiatrists, rehabilitation specialists, and other professionals [5]. The molecular mechanisms of the virus's interaction with host cells, including the processes of adhesion, penetration, replication, and release of virions, are of particular interest. The analysis of immunopathological processes, particularly the cytokine storm phenomenon, is equally important, as it is one of the key factors determining the severity of the course and prognosis of the disease [6].

Currently, despite ongoing clinical trials of safe and effective antiviral drugs and the acceleration of vaccine development programs, the risk of long-term complications caused by the SARS-CoV-2 infection is increasing. Neurological and depressive disorders and their connection to COVID-19 are a pressing neurological problem that needs to be addressed [7].

The impact of COVID-19 on the central nervous system (CNS) has not been fully studied. Therefore, medicine still cannot say exactly which patients have nervous system dysfunction and when the body can recover. COVID-19 complications lead to damage to organs and tissues with a prolonged course, as well as exacerbation of chronic diseases such as diabetes, venous insufficiency, hypertension, asthma. It is noted that the neurotropic virus enters the nervous system through olfactory receptors in the upper part, directly damaging the limbic system, hypothalamus, cerebellum, and respiratory centers. The search for a solution to the features of diagnosis and treatment of cerebro-asthenic syndrome after COVID-19 is one of the complex and urgent problems of modern neurology[8].

Worldwide, a number of scientific studies are being conducted to optimize the features of diagnosis and treatment of cerebro-asthenic syndrome after COVID-19. In this regard, scientific research aimed at studying the pathogenesis of central nervous system disorders in post-COVID cerebro-asthenic syndrome and developing clinical and neurological signs, the state of cognitive functions in patients with post-COVID cerebro-asthenic syndrome according to the Zung, Beck, FSS, Sheehan, MMSE, SHAS scales, markers of inflammation and coagulopathy in patients with post-COVID cerebro-asthenic syndrome, diagnosis and treatment of patients with post-COVID cerebro-asthenic syndrome is of particular importance[9].

In our country, certain measures are being implemented aimed at developing the medical field, adapting the medical system to the requirements of world standards, including early diagnosis, treatment, and prevention of complications of somatic diseases.

Materials and methods of research. For the purpose of the study, 120 patients who were undergoing inpatient treatment at the "Geolog" Specialized Distribution Center in Qarshi, Qashqadaryo region, were examined.

All patients in the acute period of the disease underwent in-depth clinical and neurological examination, assessed the severity of the disease, the presence of severe complications of the peripheral nervous system, such as pneumonia, severe forms of respiratory failure, acute ischemic and hemorrhagic stroke.

The inclusion criteria for patients in the study were COVID-19 patients confirmed by PCR analysis, MSCT examination of the chest organs, and other analyses.

When assessing the clinical condition of patients based on the research results on a 7-point CCAS scale, they were divided into groups, for which we conducted 12-week observation.

Research results: The main group included 120 patients who had cerebral-asthenic syndrome and other neurological complications after COVID-19. The control group included 30 conditionally healthy individuals who had COVID-19 and had no neurological disorders after 12 weeks.

All examined patients of the main group were divided into 3 groups: the 1st group consisted of 45 patients with COVID-19 and asthenic syndrome complicated by COVID-19, the 2nd group consisted of 35 patients with chronic anxiety syndrome complicated by COVID-19. The 3rd group included 40 patients with COVID-19 complications manifested as complex manifestations of cerebral asthenia and anxiety syndrome.

The reason for dividing the main group of patients into groups in this form was that in our study, we determined what biochemical and psychological disorders occur in various neurological disorders induced by COVID-19 complication syndrome. When studying 120 patients included in our observation, dividing them into different age groups, patients aged 18-44 years comprised 41 (34.2%) people, patients aged 45-59 years comprised 57 (47.5%) people, patients aged 60-74 years comprised 22 (18.3%) people. According to WHO recommendations for age grouping in 2015, as shown in Table

2.1, in the 1st group, patients aged 18-44 years were 12 (26.6%), patients aged 45-59 years were 25 (56.6%), with the largest number of patients being 60-74 years - 8 (17.8%). Their average age was 48.8 ± 3.8 years. In the 2nd group, the main patients were 18-44 years old (15 people 42.8%), while patients aged 45-69 and 60-74 years comprised 14 (40%) and 6 (17.2%) respectively. The average age of this group was 43.8 ± 4.5 years. In the 3rd group, patients aged 45-59 years (45%) predominated, patients aged 18-44 years comprised 14 (34%), patients aged 60-74 years comprised 8 (20%). The average age of the 3rd group was 46.9 ± 4.8 years. Also, out of 120 examined individuals, 55 (45.8%) were women and 65 (52.2%) were men.

Patients were assessed using the cognitive status assessment mini-test (Mini-mental State Examination- (MMSE) (1975), fatigue assessment scale - FSS (Fatigue Severity Scale), Zung depression scale (Zung Self-Rating Depression Scale (1971)), and Beck depression questionnaire (Beck Depression Inventory 1996), Sheehan scale (Devda Sheehan Self-Assessment of Anxiety Scale (1983)) to determine the presence of anxiety in patients, SHAS (Asthenic State Scale) to conclude the presence of an asthenic state. Through conducting these studies, we were able to draw conclusions about the degree of neuro-inflammatory process in the CNS in patients during the acute period of COVID-19 and after the disease, and to select patients with cerebro-asthenic syndrome. The Shihan scale was used for screening and diagnosing the anxiety spectrum in adults. Using this scale, anxiety disorders and somatic and autonomic manifestations of panic attacks are identified according to various criteria. The presence of these characteristics was assessed using the Sheehan scale using numbers from 0 to 140.

During the study, among all patients observed in the main group, patients with a predominance of cerebro-asthenic symptoms among neurological disorders in terms of clinical course constituted 37.5% ($n=45$), patients with a predominance of chronic anxiety - 29.2% ($n=35$) and patients with similar neurological symptoms in combination - 33.3% ($n=40$) and were divided into groups accordingly (I group of cerebro-asthenia, II group of anxiety, III mixed). Also, in all the listed groups and conditionally healthy examined individuals, various neurological studies were conducted, in particular, the SAN and MMSE scale for assessing general and cognitive status, the SHAS and FSS scales for assessing asthenic status and chronic fatigue, the Beck and Zung scales for assessing depression in the examined patients, the Sheehan scale for assessing anxiety, thereby checking the presence of additional cognitive-neurological disorders and for which group these disorders are more characteristic. All neurological studies used showed a normal indicator in the control group, which confirms the absence of neurological and cognitive disorders in the conditionally healthy examined individuals without clinical signs of COVID-19 complication syndrome.

On the other hand, the observed changes in all groups showed a statistically significant difference compared to the control group ($p < 0.05$) and indicate a significant change in the neurological and cognitive-functional status of patients with clinical signs of COVID-19 complication syndrome.

If we compare the indicators of the groups with various neurological disorders, then in group I, as expected, higher indicators were revealed according to the SAC and FSS scales (scales that help determine the presence of signs of chronic fatigue - asthenia and its degree). According to him, the FSS scale showed the presence of chronic fatigue and weakness in this group, and the SAC indicator - the presence of extremely pronounced asthenic syndrome. Similarly, the III group also showed a result close to the indicator of the I group on the SAC scale, but statistically significantly lower (27%) on the FSS scale (although this did not change the overall result, i.e., if we conclude about the third group on the FSS scale, then the signs of chronic fatigue and weakness were positive).

On the other hand, according to the presented scales, group II had a relatively low indicator. According to the interpretation of the obtained results, group II was positive for signs of chronic fatigue and weakness (result $FSS > 36$), and for the degree of asthenia in this group, moderate asthenia was used (result $SAC = 82.2 \pm 2.05$).

Conclusions: Thus, according to the results of the Sheehan scale, as expected, the highest result was revealed in group II with a significant and statistically significant difference compared to other groups, which indicates the presence of pronounced anxiety disorders in patients of group II. On the other hand, compared to group II, the result was almost 2.64 times lower in group I and 1.77 times lower in group III. This means that in the first group, there are no anxiety and anxiety disorders, and in the third group, there are moderately pronounced anxiety and anxiety disorders. Also, according to the results of the Zung and Beck scales used to determine the presence and degree of depression in patients in the specified groups, mild depression (according to the Zung scale), depression developed at the borderline (according to the Beck scale) was revealed in group I. In patients of group II, moderate depression was found according to the Beck and Zung scales. And finally, in group III, severe depression according to the Zung scale and severe depression according to the Beck scale were revealed. According to the results of the MMSE test used to assess cognitive activity, the indicators obtained from groups I, II, and III confirmed the presence of cognitive dysfunction in them. Also, taking into account that the severity of COVID-19 disease depends on age, we divided the patients of the main group into age groups and determined the age difference in the number of neurological indicators examined and in which age group, which types of neurological examination methods changed more.

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