Neurological and neuropsychological post-covid complications

Katarzyna Mielniczek¹, Aleksandra Kowalska², Katarzyna Jóźwik², Marta Lipiec³, Diana Dolomisiewicz⁴

¹ Students' Scientific Group at the Department of Epidemiology and Clinical Research Methodology, Medical University of Lublin

² Student Scientific Group at the Department of Neurosurgery and Pediatric Neurosurgery, Medical University of Lublin

³ Student Research Group at the independent Laboratory of Functional Disorders of the Chewing Organ, Medical University of Lublin

⁴ Student Scientific Group at the Department of Otorhinolaryngology, Head and Neck Surgery, Medical University of Warsaw
Abstract
Introduction: COVID-19 is an acute respiratory disease caused by the SARS-CoV-2 virus. It attacks the respiratory system in particular, however, it can also lead to gastrointestinal or neurological diseases. The disease leads to numerous neurological complications.
Material and method: the purpose of this study is to review the neurological and neuropsychological complications that have arisen as a result of COVID-19 outbreak. The literature available on the PubMed scientific platform was reviewed. Time descriptors were set for 2020-2022.
Results: Neurological symptoms are mainly due to cerebral hypoxia due to respiratory failure. These include encephalitis, meningitis, encephalopathies, seizures, disorders of consciousness, smell, taste and vision, among others. Neuropsychological complications can also occur.
Conclusions: Pulmonary abnormalities, neurological complications and exercise intolerance were frequently identified complications among COVID-19 survivors. The main neurological symptoms reported were fatigue, concentration changes, memory loss, and sleep disturbances. In contrast, the longest-lasting complications were fatigue, loss of concentration or memory, weakness, pain and dizziness.

Keywords: COVID-19, postcovid neurological symptoms, neurological complications.

1. INTRODUCTION
COVID-19 is an acute respiratory illness caused by the SARS-CoV-2 virus that was first detected in the city of Wuhan, China in December 2019. It was named a global pandemic by the World Health Organization (WHO) on 11th March 2020 [1]. As of today (12.05.2022), 519 million infections have been confirmed, including 6 million in Poland, of which 6.26 million patients ended in death (116,000 in Poland).
Coronaviruses are viruses belonging to the subfamily Coronavirinae, of the Family Coronaviridae, which have their genetic material encoded in RNA and are characterised by having an envelope. We distinguish between alpha-, beta-, gamma- and deltacoronaviruses. They especially attack the respiratory system, but can also lead to gastrointestinal or neurological diseases [2]. The infection is suspected on the basis of physical symptoms such as fever, cough and breathing difficulties. Subsequently, the diagnosis is further expanded with the molecular reverse transcription polymerase chain reaction (RT-PCR) test. Neurological symptoms are mainly caused by cerebral hypoxia due to respiratory failure [3]. These include encephalitis, meningitis, encephalopathies, seizures, disturbances of consciousness, smell, taste and vision [4,5]. These complications have been termed post-acute COVID-19 syndrome. The syndrome includes complications beyond the duration of the initial illness and after recovery from SARS-CoV-2 infection.
2. **Objective, material and method**
The aim of this study is to review the neurological and neuropsychological complications that have arisen as a result of COVID-19 intercourse. The literature available on the PubMed scientific platform was reviewed. Searches were performed using the following keywords: "COVID-19", "postcovid neurological symptoms", "neurological complications". Time descriptors have been set for 2020-2022.

3. **Discussion**

1. **Encephalitis**
It is diagnosed by examination of cerebrospinal fluid obtained by lumbar puncture. Patients report disturbances of consciousness, fever, convulsions or movement disorders. One of its causes is viral infection, including SARS-CoV-2 virus infection [6]. The first such case was reported in February 2020, where neuroinvasive potential was confirmed by magnetic resonance imaging. MRI showed abnormal images in the medial temporal lobe, including the hippocampus, suggesting a diagnosis of encephalitis [7].

2. **Meningitis and encephalopathy.**
SARS-CoV-2 infection can also lead to meningitis and encephalopathy, which starts with an inconspicuous headache and fever. This is followed by neck stiffness. More life-threatening symptoms include sensory disturbances, agitation, convulsions and even coma, which are indicative of progressive cerebral involvement [8]. In a 24-year-old patient diagnosed with COVID-19 disease along with the associated symptoms mentioned above, laboratory tests revealed leukocytosis, lymphopenia, neutrocytosis and elevated CRP [8,9]. A lumbar puncture was also performed and the presence of SARS-CoV-2 virus-specific RNA was detected in the collected cerebrospinal fluid. Similar symptoms were found in another patient in the course of coronavirus infection [10]. Classically, treatment begins with ceftriaxone, vancomycin, followed by antiviral drugs such as acyclovir, and in case of convulsions - levetiracetam. More severe cases additionally require steroids [8,9,10].

3. **Cerebral circulatory disorders**
With longer hospitalisation, the likelihood of cerebrovascular incidents due to SARS-CoV-2 infection increases, and in most cases they are associated with acute respiratory distress syndrome (ARDS). Patients with a history of stroke or with comorbidities (hypertension, diabetes) are more at risk [8]. It has also been reported that COVID-19 can cause ischaemic stroke accompanied by elevated D-dimers and troponin levels. Increased levels of pro-inflammatory cytokines cause hypercoagulability of the blood, which may result in cerebral vasculitis and a more severe course of infection [11].
4. Epilepsy
An epileptic seizure in the course of COVID-19 may be a symptom of virus entry into the central nervous system, but pneumonia leading to hypoxaemia and subsequent brain damage may be an cause of seizures. In patients with epilepsy, an increase in seizure frequency may occur as a result of infection due to a lowered threshold through the fever [12]. Abnormal EEG or epileptic seizures occurring in patients with severe infection are caused by electrolyte and metabolic imbalances, so control of these imbalances is important in treatment. Respiratory exercises and maintenance of the respiratory system are aimed at avoiding hypoxia leading to seizures [13]. If COVID-19 disease is accompanied by a clinical or subclinical epileptic seizure or status epilepticus, the cause ought to be identified and treatment initiated as soon as possible. It is also often necessary to start treatment with antiepileptic drugs to interrupt prolonged seizures and to prevent further seizures. For seizures lasting less than 5 minutes, there is no need for short-term use of benzodiazepines, but anticonvulsants are recommended to prevent further seizures. Care should be taken when selecting drugs as antiepileptic drugs can have serious interactions with COVID-19 adjunctive medications. For example, lacosamide prolongs the PQ interval and hydroxychloroquine prolongs the QT interval in the electrocardiogram. When administering both drugs simultaneously, caution should be exercised and the ECG monitored. Also QT interval prolongation may occur with azithromycin and chloroquine, and some antiepileptic drugs (e.g. carbamazepine, lacosamide, phenytoin and rufinamide) may cause cardiac conduction disturbances. In this case too, caution should be exercised and the ECG monitored [14].

5. Guillain-Barré syndrome
A study was conducted among COVID-19 patients and found 11 cases of Guillain-Barré syndrome among 2500 patients. In these patients, complications could persist for quite a long time and even lead to death. Guillain-Barré syndrome usually develops in the acute phase of infection. The clinical picture varies from mild symptoms, such as reduced muscle strength in the limbs, paresthesias or facial paralysis, to respiratory muscle involvement. As part of the treatment, rehabilitation should be implemented, which should be determined according to the severity and the regions affected. The best progress has been shown with motor stimulation exercises to restore muscle tone, training to restore facial mobility in case of paralysis, or in case of greater severity, breathing exercises and external stimulation with robotic tools [13].

6. Loss of smell and taste
These are some of the most common symptoms in the course of Coronavirus infection. They are most often transient, with restoration of smell and taste after several days to weeks, but anosmia differs in its sudden onset and rapid return. Smell has been shown to disappear slightly earlier (peak on day 3) than taste (peak on days 5-7). The olfactory epithelium contains cells that accumulate virus after infection. ACE2 is expressed in the epithelial cells of the tongue but probably not in the taste buds, but drugs that inhibit ACE2 cause taste disturbances. In the olfactory epithelium, evidence suggests a distinct cascade of cellular events that may explain the transient anosmia in COVID-19. Chemosensory deficits are usually transient and last from a few days to about 2 weeks; however, in a significant number of patients they may remain as a complication for a long time [15].
7. Neuropsychological complications
The most common is PTSD, or post-traumatic stress disorder. It is most often caused by stress related to the stay in the ICU and the entire hospitalization [16,17]. It occurs more frequently in women than in men, in young people, and even more frequently in patients burdened with psychiatric illnesses [18,19]. Another common complication is depression and anxiety. Moreover, the severity of anxiety reported by older survivors was lower than in younger people, and there was no difference in the severity of depressive symptoms according to the age of patients [17]. Subsequently, memory impairment was found. These disorders ranged from moderate to severe memory impairment [16,19]. Insomnia, sleep disturbances, stigma and concentration problems have been reported among recovering patients [17].

4. Summary
COVID-19 can cause several types of complications after recovery. Pulmonary abnormalities, neurological complications, and exercise intolerance were frequently identified complications among COVID-19 survivors. The main neurological symptoms reported were fatigue, concentration changes, memory loss, and sleep disturbances. In contrast, the longest lasting complications were fatigue, loss of concentration or memory, weakness, headache and dizziness. It is important to be aware that complications do occur, but the most important thing is to start treating them as soon as possible.

References: