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COVID-19 PANDEMIA: NEUROPSYCHIATRIC COMORBIDITY AND CONSEQUENCES

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SUMMARY

Infection with the new corona virus (SARS-CoV-2) was first registered in December 2019 in China, and then later spread rapidly to the rest of the world. On December 31, 2019, the World Health Organization (WHO) informed the public for the first time about causes of pneumonnia of unknown origin, in the city of Wuhan (Hubei Province, China), in people who were epidemiologically linked to a seafood and wet animal whole sale local market in Wuhan. Coronavrus disease, called COVID-19 (Corona virus disease 2019), after China quickly spread to most countries in the wold, and the WHO on March 11, 2020 declared a pandmic with this virus. SARS-CoV-2, has a high level of sequential similarities to the SARS-CoV-1 and uses the same receptors when it enters the human body (angiotensin-converting enzyme 2/ACE2). COVID-19 is respiratry infection that is primarily transmitted via respiratry droplets. Typical symptoms of COVID-19 infection can be very moderate (infected can be even asymptomatic) to very severe, with severe respiratory symptoms (bilateral severe pneumonia), septic schock, and fatal outcome. Numeous unknows regarding the biological, epidemilogical adn clinical characteristics of COVID-19, still exist, and make it impossible to predict with certainty the further course of the current pandemic.

COVID-19 is primarily a disease of the respiratory system, but SARS-CoV-2, in a number of patients also penetrates the CNS, and apparently could be responsible for fatal outcome in some cases. The entrry of the virus into the brain can lead to neurological and psychiatric manifestationss, which are not uncommon, including headache, paresthesia, myalgia, impaired consciousnessm, confusion or delirum and cerebrovascular diseases.

SARS-CoV-2 positive individuals should be evaluated in a timely manner for neurological and psychiatic symptoms because tretament of infection-related neurological and psychiatric complications is an important factor in better prognosis of severe COVID-19 patients.From the current point of view, it seems that in COVID-19 survivors, in the coming years and decades, the inflammatory systemic process and/or the inflammatory process of the brain could trigger long-term mechanisms that generally lead to an increase of neurological and neurodegenerative disorders.

Psychosocial consequences as well as consequences for mental health are also significant, both for the general population and especially for health workers of all profiles.

COVID-19 pandemia is associtaed with negative psychosocial consequences, including depressive symptoms, anxiety, anger and stress, sleep disorders, simpotms of posttrauamtic stres disorder, social isolation, loneliness and stigmatization.

Key words: *COVID-19 – SARS-CoV-2 – neuropsychiatric comorbidity – neurological manifestations – psychiatric disorders – mental health*

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BASIC CHARACTERISTICS OF THE VIRUS, ETIOPATHOGENESIS, EPIDEMIOLOGY

Infection with the new corona virus (SARS-CoV-2) was first registered in December 2019 in China, and then later spread rapidly to the rest of the world. On December 31, 2019, the World Health Organization (WHO) informed the public for the first time about causes of pneumonnia of unknown origin, in the city of Wuhan (Hubei Province, China), in people who were epidemiologically linked to a seafood and wet animal whole sale local market in Wuhan (WHO 2020). Coronavirus disease, called COVID-19 (Corona virus disease 2019), after China quickly spread to most countries in the wold, and the WHO on March 11, 2020. declared a pandmic with this virus (Ghebreyesus 2020). In Bosnia and Herzegovina, the first infected person was registered on March 9, 2020 in the city of Konjic.

SARS-CoV-2 is therefore a new, previously unkown corona virus, with a single strand of ribonucleic acid (RNA virus), classified as a type of SARS-related virus (SARS-CoV), subgenus Sarbecovirus, genus Betacoronavirus, subfamily Orthocoronavirinae, family Coronaviridae, line Nidovirales (Cui et al. 2020). To date, seven types of human coronavirus have been identified, four of which cause moderate symptoms of upper respiratory tract infection, while two called SARS-CoV and one called MERS-CoV, have caused large epidemics with a significant percentage of severe clinical pictures and fatal outcome. It is almost certain that SARS-CoV-2, like other simiar viruses, is of animlar origin, but it is not yet clear which animal is the primary source, and how the virus was transmitted to humans. The SARS-CoV-2 that leads to COVID-19 is gene different from the severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1) and the Middle East respiratory syndrome corona virus (MERS-CoV), which were previously the cause of two epidemic waves in the world.

These viruses have similar receptor sites that bind to angiotensin converting enzyme 2 (ACE2)(SARS-CoV-1 and SARS-CoV-2) and CD26 (MERS/SARS-CoV-2), respectively (Khan et al. 2020; Vankadari and Wilce 2020). Differences in the gentic sequence and molecular pathways of human cell infection with SARS-CoV-2 comapred to other related viruses are most likely the biological basis of different epidemiological characteristics and clinical manifestations of COVID-19 in relation to other related diseases such as severe acute respiratory sndrome (SARS) from 2002 and respiratory syndrome of the Middle East (MERS) from 2012 (Milovanović et al. 2020).

COVID-19 is respiratry infection that is primarily transmitted via respiratry droplets. The primary route of transmission is close contact with a person who has the virus, especially during coughing, sneezing, and medical interventions in the respiratory tract, such as intubation, tracheobronchial aspiration, and mechanical ventilation (Chan et al. 2020). SARS-CoV-2 molecules have been isolated from the blood, saliva, tears, conjuctival fluid and stool of patients, so there is a possibility of transmitting the infection through these routes too.

Experiments have shown that SARS-CoV-2 stays in the aerosol for up to three hours, on the copper surface for up to four hours, on carboard for upt to 24 hours, and for 2-3 days on plastic and stainless steel, which is a dynamics very similar to in a related, SARS-CoV-1 virus (van Doremalen et al. 2020). SARS-CoV-2 is extremely contagious to the human species, significantly more than SARS-CoV-1 and MERS-CoV viruses which may, at leaset in part, explain its significantly higher, pandemic potential (Milovanović et al. 2020). In one study, it was found that there were about one third of asymptomatic forms of the disease, and in one large, closed group, on average about 17.9% (15.5-20.2%) (Nishiura et al. 2020, Mizumoto et al. 2020). It has been estimated that the infectious period probably begins shortly before the onset of symptoms and lasts 7-12-days in moderate and up to two weeks in severe cases of COVID-19 (Woelfel et al. 2020). Decontamination is significantly faster in mild than in severe forms of COVID-19. In one study of hospitalized patients, 90% of those with mild illness had a negative viral infection test as early as day 10, and on the other hand, in all severe cases, 39% (77% of them were treated in the intensive care unit) on day 10 and after that the test remained positive (Liu et al. 2020).

BASIC CLINICAL PICTURE

Typical symptoms of COVID-19 infection can be very moderate (infected can be even asymptomatic) to very severe, with severe respiratory symptoms (bilateral severe pneumonia), septic schock, and fatal outcome. The most common symptoms of COVID-19 patients are fever (83-95% of patients), dry cough (57-82%), exhaustation (29-69%), sputum expectoration (26-33%), dyspnoea (18-55%), sore throat (5-17%), headache (13.6%), myalgia and arthralgia (14.8%), fever (11.4%), dizziness (9-12%), confusion (9%), rhinorrhea (4-5%), nasal congestion (4.8%), gastrointestional symptoms such as nausea, vomiting and diarrhea (1-10%), haemoptysis (1-5%) and conjunctival congestion (0.8%) (Milovanović et al. 2020. Guan et al. 2020, Chen et al. 2020, Huang et al. 2020, Wang et al. 2020, Sun et al. 2020, Rodriguez-Morales et al. 2020, Li et al. 2020, Lu et al. 2020a, Cai et al. 2020).

High temperature can occur continuously or intermittently, with or without fever. The cough is usually unproductive. Chest pain may suggest the presence of pneumonia, while gastrointenstinal symptoms may precede the onset of fever and dysponoea for one to two days. In one group of patients, erythematous rash (15.9%), generalized urticaria (3.4%) and vesicular rash (1.1%) were observed (Recalcati 2020). Atypical manifestations at the beginning of the disease, such as fatigue without fever and respiratory symptoms; hemoptysis or anosmia and ageusia, are not so rare; they can may make it difficult to make an accurate diagnosis in a timely manner and to take appropriate epidemiological measures (Hao et al. 2020; Shi et al. 2020; Vaira et al. 2020).

According to the WHO (2020b), COVID-19 is classified into four forms: mild disease, pneumonia, severe pneumonia and acute respiratory distress syndrome. The basic criteria for classification are based on the status of ventilation and oxygenation, radiological findings on the lungs and the presence of symptoms and signs that indicate a disorder of the general condition. One of the reports notes that the critical cases of COVID-19 were mostly elderly (average age 70 years), of which 86% had comorbidities, all had acute respiratory distress syndrome (ARDS), mechanical ventilation was applied in all, and the mortality was 67% (Arentz et al. 2020).

INVOLVEMENT OF THE CENTRAL NERVOUS SYSTEM

The high pathogenicity of coronavirus (CoV) infection is well known from previous epidemics – Severe Acute Respiratory Syndrome (SARS) caused by SARS-CoV-1 and Middle East Respiratory Syndrome (MERS) caused by MERS-CoV. The new coronavirus, SARS-CoV-2, has a high level of sequential similarities to the SARS-CoV-1 and uses the same receptors when it enters the human body (angiotensin-converting enzyme 2/ACE2) (Lu et al. 2020b, Wan et al. 2020). The MERS-CoV virus eneters via dipeptidyl peptidase 4 (DP4), which is present in the lower respiratory tract, kidneys, small intenstine, liver, and immune system cells (Mattern et al. 1991, Boonacker & Van Noorden 2003).

We do not yet know the exact route by which SARS-CoV or MERS-CoV enters the central nervous system (CNS). However, a haematological or lymphatic pathway does not appear to be possible, especially in the early stages of infection, since viral particles are not detected outside neurve cells in infected brain areas (Ding et al. 2004, Gu et al. 2005, Xu et al. 2005). On the other hand, there is evidence that coronaviruses attack peripheral nerve endings and reach the CNS via nerve synapses (Li et al. 2012, 2013, Matsuda et al. 2004).

Experiments on mice have demonstrated that SARS-CoV probably enters the brain via the olfactory bulb, and then spreads to other specific parts of the brain such as the thalamus and brainstem through the olfactory nerves. Similar was demonstrated for MERS-CoV. Interestingly, MERS-CoV was infectious in small doses only to the brain but not to the lungs and this brain infection correlated with high mortality in experiemental mice. All these studies indicate that the brainstem is one of the highly susceptible areas for infection with SARS-CoV and MERS-CoV viruses. Although this hypothesis requires additional validation for SARS-CoV-2 infection, the fact that almost 50% of COVID-19 patients have neurological problems including epilepsy, ischemic and hemorrhagic stroke, cannot be ignored (Gandhi et al. 2020).

SARS-CoV-2 is therefore responsible for the current COVID-19 pandemic with far more infected and dead than during the 2002 and 2012 epidemics, respectively (WHO 2020c; WHO 2019). Despite the short duration of the current pandemic, several neurological and neuroradiological phenotypes have already been reported, prompting an urgent approach to investigating the mechanisms and etiology behind the association of SARS-CoV and the CNS; and several laboratories have already studied SARS-CoV in a number of animal species, including primates, mice, rats, hamsters, and moss (WHO 2004, Callaway et al. 2020).

The onset of severe acute respiratory syndrome in Guangdong Province, China, led to the discovery of SARS-CoV-1, highly pathogenic virus that led to the SARS epidemic (Xu et al. 2005). Although this virus is primarily respiratory, there have been reports of neurological manifestations, such as epileptic seizures and encephalitis, suggesting CNS involvement by infection (Natoli et al. 2020; Ksiazek et al. 2003; Hung et al. 2003). Following these clinical studies, several post-mortem neuropathological studies have detected SARS-CoV N protein and RNA gene fragments in the neurons of infected patients and pathological changes, such as brain tissue edema and cerebral venous vasculitis (Lau et al. 2004).

Thus, the neuroinvasive predisposition of coronaviruses as their common feature has been clearly demonstrated in previous studies.In the light of the high similarity between SARS-CoV-1 and SARS-CoV-2, it can be concluded that SARS-CoV-2 has similar potential to enter the CNS. Furthermore, epidemiological monitoring of COVID-19 showed that the median from the first symptom to dyspnea was five days, to hospital admission seven days, and to intensive care unit addmision eight days (Wang et al. 2020). This means that the latent period is sufficient for the virus to penetrate and damage the medullary neurons.

NEUROLOGICAL MANIFESTATIONS

The first published studies indicated that some patients infected with SARS-CoV-2 have neurological disorders, such as headache (about 8%), nausea and vomiting (about 1%)(Chen et al. 2020; Talbot et al. 1993; Dube at al. 2018). Furthermore, Mao et al. (2020) found that about 40% of patients among those with a severe clinical picture had neurological manifestations including cerebrovascular diseases and confusion.

Today, we know for sure that coronaviruses are not only limited to the respiratory tract, but can also affect the CNS, leading to neurological disorders (Li et al. 2020). This neuroinvasive predisposition to coronavirus has been documented for almost all beta-coronaviruses, including SARS-CoV-1, MER-CoV, HcoV-229E, HcoV-OC43, as wll as others (Li et al. 2016; Talbot et al. 1993; Dubé et al. 2018).

In the current dramatic COVID-19 pandemic, caused by SARS-CoV-2, the highest registered mortality in Europe, on May 12, 2020, expressed as the number of deaths per million inhabitants, ranges from 301 in Ireland, 322 in Netherlands, 328 in Sweden, 756 in Belgium to 1208 in San Marino (408 in France, 482 in UK, 511 in Italy, 576 in Spain, 621 in Andora) or as a percentage of deaths per number with confirmed infection averaging 6.9%. In the USA, the number of infected is the highits in the world, and the number of deaths per million inhabitans is 249. In the countries in the region (ex Yugoslavia), expressed in the same way, the number of deaths is the highest in Slovenia – 49, and the lowest in Montenegro – 14 (Croatia - 22, Serbia - 25, Bosnia and Herzegovina – 36, Northern Macedonia – 44) (https://epidemic-stats.com 2020).

In this pandemic as wll as in SARS and MERS, respiratory symptomatology is the most prominent (WHO 2020b). However, as we have already mentiend, neurological phenotypes are already being registered, which affect both the central and peripheral nervous system, leading to anosmia, ageusia, necro-hemorrhagic encephalitis, Guillain-Barre syndrome (Ding et al. 2004, Poyiadji et al. 2020, Zhao et al. 2020, Toscano et al. 2020, Gautier & Ravussin 2020).

According to the already mentioned study of colleagues from China (Mao et al. 2020), based on the analysis of 214 hospitalized patients in three hospitals in the city Wuhan (with comfirmed COVID-19 infection), 88 of them (41.1%) were seriously ill and 126 (58.9%) were with moderate symptoms. Severe patients were older (58+/-15.0 years) than those with a moderate clinical picture (48.9+/-14-7 years), and had more comorbidities (42 or 47.7%) than those with moderate symptoms (41 or 32.5%); the most common was elevated blood pressure (32 or 36.4%). They showed less typical symptoms such as fever (40 or 45.4%) as opposed to those with a moderate clinical picture (92 or 73%) and cough (30 or 42%); those with a moderat clinical picture coughed in 77 (61.1%) cases. Of the total number analyzed, 78 (36.4%) had neurological manifestations. Neurological manifestations were more frequent in those with a more severe clinical picture (40 or 45.5%) compared to those with a moderate one (38 or 30.2%). The most common neurological disorders were acute cerebrovascular disease – 5 (5.7%), disturbance of consciousness (13 or 14.8%), skeletal muscle damage (19 or 19.3%). Those with a moderate clinical picture also had neurological manifestations, but less in frequency (Mao et al. 2020).

One retrospective study, following an outbreak of infection in Wuhan (China), found a stroke incidence among hospitalized patients due to COVID-19 of about 5%, with the youngest patient in that series being 55 years old (Li et al. 2020). Furthermore, five patients from the New York City, under the age of 50 (37, 39, 44, and 49 years) with a stroke involving large blood vessels who had severe acute respiratory syndrome, were recently presented, caused by SARS-CoV-2 (Oxley et al. 2020).

Due to the observed fact that SARS-CoV-2 infection may also have neurological symptoms, Wua et al. (2020) emphasize that CoV positive individuals should be evaluated in a tiemly manner for neurological symptoms, including headache, impaired consciousness, paresthesias, and other neurological signs, and treatment with infection associated complications are an imporant factor in better prognosis of severe forms of COVID-19 patients.

De Felice et al. (2020) in their recent review articel on the association between COVID-19 and CNS, concluded that new evidence suggests that SRS-CoV-2 is associtated with neurologic changes in COVID-19 patients with a severe clinical picture. There are three possible scenarios: 1) direct impact of SARS-CoV-2 on the CNS with neuroligical disorders; 2) worsening of existing neurological disorders; 3) increased risk of neurologicl disorder for other reasons. Given the global dimension of the current pandemic and the high transmissibility of the SARS-CoV-2 virus, the evidence that already exists about the association between this virus and the CNS, raises concerns about the potential long-term effects of COVID-19 on the CNS. The authors propose monitoring of patients who have survived COVID-19, including careful imaging, laboratory, and clinical neurological evaluation, to determine the extent to which the interrelatonship between systemic infection and CNS infection leads to CNS damage and neurological disordes. From the current point of view, it seems that in COVID-19 survivors, in the coming years and decades, the inflammatory systemic process and/or the inflammatory process of the brain could trigger long-term mechanisms that generally lead to an increase of neurological and neurodegenerative disorders.

SARS-CoV-2 is a new strain of coronavirus that has shaken the planet ina way that has not been seen since the great flu pandemic, the so-called Spanish fever, which was in 1918. Numerous unknowns regarding the biological, epidmeiological, and clincal characteristich of COVID 19, which still exist, make it impossible to predict with certain the further course of the current pandemic (Milovanović et al. 2020).

PSYCHIATRIC DISORDERS AND CONSEQUENCES

Many hospitalized COVID-19 patients may develop delirium, which may be related to the postulated pathophysiology of the virus, which indicates the possibility of virus invasion of the brainstem, as well as well as to inerventions that are regularly used in the tretament of these severe patients. This fact represents a particular challenge in the prevention and treatment of delirium, especially in intenisve care units (ICUs). In addition to the neurobiology of the SARS-CoV-2 and the atypical delirium factors present in ICU, the current pandemic has created circumstances of extreme isolation and distancing from human contact, including loved ones, all affecting the onset of this neuropsychiatric disorder (Kotfis et al. 2020).

In the aforementioned retrospective study by Mao et al. (2020) which included 214 COVID-19 patients, disturbance of consciousness was present in about 15% of patients. Kotfis et al. (2020) point out that earlier reports from China speak of an incidence of encephalopathy of 25%, but that it is certainly an underestimated frequency because, as experts in the field of intensive care they know that this is the case whenever delirium is not monitored properly.

Due to the fact that iformation about the diseas caused by SARS-CoV-2 (COVID-19) spread very quickly, becoming pandemic even before the virus pandemia (infodemia), and after the disease spread outside China, confirming the remarks that it is very contagious disease, but also a fatal disease, the general public has become very upset (Dong et al. 2020; Jakovljevic et al. 2020). Apart from respiratory and neurological disorders, it was inveitable to expect that such a large pandemic with numerous uncertainities, drastic changes in everyday life among a significant number of inhabitans of the panet, and even our country would lead to psychological difficulties for a significant number of population, including health workers.

Among the first reports is a study by Xia et al. (2020) who analyzed the presence of stress sympotms, anxiety and sleep quality, and the impact of social support on these symptoms, in 170 residents in central China during the COVID-19 pandemic in January 2020 spent 14 days in self-isolation. They found a high level of stress and anxiety, as wll as poor sleep quality in most respondents, and a positive correlation in terms of their lower presence with adequate social support.

According to a study by Liu et al. (2020) who analyzed 285 respondents over the age of 18 in Whuan and surroundig cities, where the COVID-19 epidemic started in China, a month after the outbreak (the results were collected in a period of January 1 to February 2, 2020), symptoms of post-traumatic stress disorder (PTSD) were present in 7% of subjects. Women had significantly more frequent symptoms of re-experiencing, both repression and arousal, and in the domain of cognition and mood. Subjects who had better sleep quality also had fewer symptoms of PTSD. The authors note that this is the first study on this topic and remind that in earlier study done in Taiwan, after the SARS epidemic, the incidence of depressive symptoms in the sample tested was 3.7% (Ko et al. 2006).

Healthcare professionals are certainly at high risk of being infected with SARS-CoV-2 (ECDC 2020; Tostmann et al. 2020). In our country, according to the reports of crisis headquarters, there are infected health workrers in all areas. In order to maximally protect healthcare professionals, there are recommendations both at the European level and at the level of each county, which include equipment, testing protocols, protocols for working with pateints who come to healthcare facilities, etc. (ECDC, 2020). However, this is of course not carried out in the same way in all regions and countries, and in addition to typical respiratory and neurological sympotms, symptoms of stress and mental disorders can be expected among healthcare workers. So far, there are not many studies related to the current COVID-19 pandemic and its consequences for mental health.

Previous studies have shown that health professionals developed adverse psychological reactions during infection with the SARS-CoV-1 (Maunder et al. 2003, Bai et al. 2004, Lee et al. 2007). A Toronto study, analyzing the reactions of hospitalized people to SARS and health workers at a large hospital found, that SARS patients showed fear, loneliness, bordom, and anger, and were concerned about the possibel consequences of quarantin and infection on members family and friends. They showed concern about fever and insomnia. Employees, on the other hand, expressed fear of their own infection, infection of family members, friends and colleagues. The care (of health care workers) about health care workers as patients was emotionally difficult for them, and uncertainity and stigmatization were highlighted phenomena and topics of conversation, both among patients and among health care professionals (Maunder et al. 2003).

According to a study from Hong Kong that analyzed the psychological consequences among health workers, a year after SARS infection (SARS-CoV-1), they found that the stress level was still high. The authors emphasize that the psychological implications of infectious diseases (in this particular case SARS infection) should not be ignored and that mental health experts should have a role to play in the rehabilitation process (Chua et al. 2004).

Maunder (2004), studying the psychological consequences of the SARS epidemic in the first half of 2003 in Canada, nots that it was an unpredictable trauamtic event for health workers in Toronto and that they learned some lessions from it. It is estimated that 29-35% of health workers have experienced a high level of distress. The nurses were in the greatest distress, then those who had contact with SARS patients and those who had children. The lessons they have learned are: efforts are needed to mitigate the psychological impact of actions in controlling infection, especially the interpersonal distance that these actions have promoted; effective risk information and education is a priority in the early stages of the epidemic; health professionals can play a role in influencing good media reporting patterns, that can increase or decrease the general morale of the population; health workers need to have psychological support within the health system as well as cleare practical support that facilities their hard work during an epidemic. High scores on the impact event events in nurses, who had contact with SARS patients, and significant negative impact of social isolation and fear for health, were reported in another study from Toronto (Maunder et al. 2004).

Huang and Zhao (2020) recently published the results of study, conducted during the COVID-19 epidemic in China, based on an online cross-sectional survey that included 7.236 voluntaries. They determined the overall prevalence of generalized anxiety disorder in 35.1%, depressive symptoms in 20.1%, and sleep quality disorder in 18.2%. Compared to other peofessionals, health workers were more likely to have poorer sleep quality. Age less than 35years and focusing on the COVID-19 pandemic (TV, internet cell phone, thinking about infection and consequences) for more than three hours a day was associated with greater anxiety, and in the case of health workers with poorer sleep quality.

In review article, Röhr et al. (2020) analyzed 13 studies examining the psycchosocial consequences of quarantine measures during the COVID-19 pandemic, noting that these measures were associtaed with negative psychosocial outcomes, including depressive symptoms, anxiety, anger and stress, PTSD, social isolation, loneliness and stigmatization. Based on the analysis, the authors concluded that quarantine isolation measures during the COVID-19 pandemic have huge negative consequences for mental health; and that preventive interventional measures to reduce psychosocial consequences should be an integral part of the crisis response during pandemic conditions. The second review article, which was based on a review of 28 published papers in journal included in PubMed indexing, and which delt with the effects of the COVID-19 pandemic on menal health, it was concluded that symptoms of anxiety and depression (16-28%) and stress (8%) are common psychological reactions to the COVID-19 pandemic and are also associtaed with sleep disorders (Rajkumar 2020).

CONCLUSION

By the time I finis this text (May 12, 2020), more than 4.200.000 people worldwide have been confirmed to be infected with SARS-CoV-2, more than 284.000 people have died or due to COVID-19, which is 6.8% of those infected. Over 1.500.000 recovered were reported. These figures far exceed the SARS and MERS epidemics of 2002 and 2012 respectively.

SARS-CoV-2 is a new strain of coronavirus that has shaken the planet in a way that has not been seen since the great flu pandemic (the so-salled The Spanish flu) that was in 1918. Numeous unknows regarding the biological, epidemilogical adn clinical characteristics of COVID-19, still exist, and make it impossible to reliable predict the further course of the current pandemic.

The consequences of this pandemic on the overall life of people on the planet are significant and unthinkable. COVID-19 is primarily a disease of the respiratory system, but SARS-CoV-2, the RNA virus that causes the disease, in a number of patients also penetrates the CNS, leading to serious neurological disorders, and apparently it is also responsible for mortality. The entrry of the virus into the brain can lead to neurological and psychiatric manifestationss, which are not uncommon, including headache, paresthesia, myalgia, impaired consciousnessm, confusion or delirum and cerebrovascular diseases. Psychosocial consequences as well as consequences for mental health are also significant, both for the general population and especially for health workers of all profiles.

SARS-CoV-2 positive individuals should be evaluated in a timely manner for neurological and psychiatric symptoms, including headache, impaired consciousness, paresthesia, myalgia, cerebrovascular diseses, and other neurolgical signs, because tretament of infection-related complications is an important factor in better prognosis of severe COVID-19 patients.

From the current point of view, it seems that in COVID-19 survivors, in the coming years and decades, the inflammatory systemic process and/or the inflammatory process of the brain could trigger long-term mechanisms that generally lead to an increase of neurological and neurodegenerative disorders.

Monitoring of patients who have survived COVID-19 is imperative, including careful imaging and laboratory clinical neurological evaluation, to determine the extent to which the interrelationship betwen systemic infection and CNS infection could lead to brain damage and neurological disorders. Also, as the COVID-19 pandemic has major negative consequences for mental health, preventve interventionl approaches to mitigate psychosocial impact should be an integral part of the response to the crisis during pandemics, and the involvement of mental health professionals is likely to be required, for some time after the the pandemic passes, in order to reduce expected pospandemic psihosocial responses and mental health disorders.

I encouraga colleagues to, if they have not already begin scientific monitoring of the COVID-19 pandemic in the fields of neurology, psychiatry, and mental health in their communities.

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Osman Sinanović: concept and design of article, literature searches, writing manuscript, approval of final version.

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