Psychological and Neurological Manifestations Associated with Covid-19: a Short Review

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Background: While the COVID-19 pandemic continues to spread globally, more and more evidences are collected about the presence of psychiatric and neurological manifestations and symptoms associated with this disease. **Objective:** The aim of this short communication is to present some of psychological consequences and neurological disorders associated with the SARS-CoV-2 infections, **Methods:** This is cross-sectional study according to psychosocial and neurological manifestations caused by COVID-19 infections published in papers deposited in most influential on-line databases. **Results and Discussion:** The results show presence of central and peripheral nervous system manifestations related to coronavirus. Neurological manifestations, or NeuroCOVID, are part of the COVID-19 clinical picture, but questions remain regarding the frequency and severity of central nervous system symptoms, the mechanism of action underlying neurological symptoms, and the relationship of symptoms with the course and severity of COVID-19. **Conclusion:** The review of the published papers shows that although more and more papers are reporting neurological and psyhiatric manifestations associated with COVID-19, many items remain unclear and this uncertainty calls for a global action that requires close co-ordination and open-data sharing between hospitals, academic and public health institutions and the fast establishment of harmonised research priorities to face actual and longterm the NeuroCOVID-19 complications and psychological consequences.

Keywords: COVID-19, Neurological disorders, Psychological consequences.

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1. BACKGROUND

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 (1). In Bosnia and Herzegovina, the first infected person was registered on 5.3.2020 in Banja Luka, and in the Federation of Bosnia and Herzegovina on March 9, 2020 in Konjic.

2. OBJECTIVE

The aim of this short communication is to present some of psychological consequences and neurological disorders associated with the SARS-CoV-2 infections, and to emphasize the need a global action that requires close coordination and open-data sharing between hospitals, academic and public health institutions and the fast establishment of harmonised research priorities to face actal and longterm the NeuroCOVID-19 complications and psychological consequences.

3. METHODS

This is cross-sectional study regarding to psychosocial and neurological manifestations caused by COVID-19 infections based on facts desribed in published scientific papers searched in most influential on-line databases (PMC, Pubmed, Scopus, etc) in the year 2020.

4. RESULTS AND DISCUSSION

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)(2-4) The MERS-CoV virus enters via dipeptidyl peptidase 4 (DP4), which is present in the lower respiratory tract, kidneys, small intenstine, liver, and immune system cells (5-6). 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 nerve cells in infected brain areas (7-9). On the other hand, there is evidence that coronaviruses attack peripheral nerve endings and reach the CNS via nerve synapses (10, 11).

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 (12-14). COVID-19 results in neurological damage likely by two mechanisms; hypoxic brain injury and an immune mediated damage to the CNS.

Neurological disorders

COVID-19 is primarily a disease of the respiratory system (12). However, SARS-CoV-2, in a number of patients also penetrates the CNS, and apparently could be responsible for fatal outcome in some cases (13, 15, 16).

Site Manifestations	
Central Nervous System	Dizziness
	Headache
	Acute cerebrovascular disease Impaired consciousness Transverse myelitis
	Impaired consciousness
	Transverse myelitis
	Acute hemorrhagic necrotizing encephalopathy
	Encephalopathy
	Encephalitis
	Epilepsy
	Ataxia
Peripheral Nervous Systemm	Hypogeusia
	Hyposmia,
	Neuralgia
	Guillian Barre syndrome Skeletal muscle injury

Table 1. Neurological complications and manifestations of COVID-19

The entry of the virus into the brain can lead to neurological (NeuroCOVID-19) and psychiatric manifestationss, which are not uncommon, including headache, anosmia, ageusia, encephalopathy, encephalitis, paresthesia, myalgia, Guillain-Barre syndrome, impaired consciousness, confusion or delirum and cerebrovascular diseases (15, 17, 18). Reported neurological findings can be divided into three categories: central (headache (19, 20), dizziness (19), impaired consciousness, acute cerebrovascular disease, ataxia and seizures), peripheral (hypogeusia, hyposmia) and musculoskeletal (Table 1) (21-23). Moreover, neurological involvement in COVID-19 corresponds to three situations: a) neurological manifestations of viral infection, b) post-infective neurological complications, and c) infection in patients with neurological co-morbidity (24). According to the study of colleagues from China (18), based on the analysis of 214 hospitalized patients in three hospitals in the city Wuhan (with comfirmed COVID-19 infection), 6 of 214 patients had either ischemic or haemorrhagic strokes, although it was not reported whether the strokes occurred before or after SARS-CoV-2 infection. The most common CNS symptoms reported were dizziness (36/16.8%) and headache (28/13.1%). Furthermore, a retrospective case series from China found that 22% of people who died from COVID-19 experienced delirium compared with 1% of people who recovered (25).

Multiple cross-sectional studies have demonstrated that the incidence rate of olfactory dysfunction in COVID-19 patients varies from 33.9-68% with female dominance (26). Myalgia and muscle injury were reported in 10.7% of the cases in Wuhan (18) and rhabdomyolysis has been reported in another case from Wuhan (27). Many patients experienced hyposmia or anosmia, dysgeusia, dysarthria and either allodynia or acroparesthesias (21). So far eight cases of COVID-19 associated GBS have been reported from China, Iran and Italy (23, 28).

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 (16).

Psychiatric/psychological disorders and consequences

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

(29, 30). 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 planet, 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 Xiao et al (31) 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. 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. (32) 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, 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% (33).

Previous studies have shown that health professionals developed adverse psychological reactions during infection with the SARS-CoV-1 (34, 35). 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 (34).

Maunder (36), studying the psychological consequences of the SARS epidemic in the first half of 2003 in Canada, notes that it was an unpredictable trauamtic event for health workers in Toronto. 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 (37).

Huang and Zhao (38) 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. (39) analyzed 13 studies examining the psychosocial consequences of quarantine measures during the COVID-19 pandemic, noting that these measures were associtaed with negative psychosocial outcomes, including depressive sympotms, 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 (40, 41).

5. CONCLUSION

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 inluding headache, anosmia, ageusia, encephalopathy, encephalitis, paresthesia, myalgia, Guillain-Barre syndrome, impaired consciousness, 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. Many items remain unclear and this

uncertainty calls for a global action that requires close coordination and open-data sharing between hospitals, academic and public health institutions and the fast establishment of harmonised research priorities to face actal and longterm the NeuroCOVID-19 complications and psychological consequences.

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