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## **An Overview on Current Perspectives and Future Directions in Neurological Complications of Covid-19**

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### **Abstract**

The new threat to the human health which raised into the view named Severe Acute Respiratory Syndrome Corona virus 2(SARS-CoV-2). The virus has already been infected to more than half a million people around the world, and then it also lead to many deaths. Despite the fact that it only causes mild flu diseases in many of the patients the elderly and the children may affect badly, mortality may increase more than 15% in the above-mentioned subjects and especially with those who have multiple medical condition like, hypertension, obesity, chronic lung disease and cardiovascular disease. The most infected people will develop mild to moderate illness like fever, dry cough and

tiredness. The interesting factor involved here is, this virus has also a role as a pertinent agent for the CNS pathologies. The present pandemic gives as a call for the introduction of monitoring the changes in the health sector especially on the immune mediated neurological disorders. These changes will give us a clear idea and the measures to be taken for the interaction between the virus, the environment and the from the local communities. To fight against the present outbreak better interactions should be done between international organizations and measures for early diagnosis and treatment.

**Keywords:** Covid-19, Neurological Complications, SARS-CoV-2

### **Introduction**

The unforeseen infection which is caused by a Corona virus, is challenging to the health of the population in the world and more over to the economy. The primary outward of COVID-19 infection is pneumonia, the evidence that arise nowadays indicate that it affects the main organs other than the respiratory systems it mainly includes the Central and the peripheral nervous systems. A mounting evidence shows that neurotropism is a clear feature of corona virus<sup>[1]</sup>. The direct action on the nervous system by these viruses on the nervous tissue and by the indirect action via the triggering of immune-mediated mechanisms. In the acute phase the first action can be verified and the second only after many days, weeks, succeeding the acute phase. Corona viruses can invade the nervous tissues involving immune-functioning macrophages, microglia, or astrocytes<sup>[2]</sup>. The above mentioned observations can be considered to give specific context for the active observation to the affected individuals to try an attempt for identifying those who are at risk for developing an acute, short and long term neurological complications.

### **COVID-19 Associated Neurological Disorders: Present Findings**

The severely affected patients by the corona virus had stroke, ataxia, seizures, and low level of consciousness. In the first reports on neurological findings during the COVID-19 outbreak in Wuhan, china, neurological manifestations were present in 78/214 patients divided into 3 categories: Central nervous system (headache, dizziness, ataxia and seizure), peripheral nervous system (taste impairment, smell impairment vision impairment and nerve pain) and muscular skeletal<sup>[3]</sup>. Hypoxic encephalopathy has been diagnosed in 20% of 113 expired patients with COVID-19 virus<sup>[4]</sup>. An analysis based n 6 studies in patients with COVID-19 interestingly cerebrovascular disease was identified as a risk factor among the others like hypertension, chronic obstructive pulmonary disease, cardiovascular disease and diabetes<sup>[5]</sup>. The happening of cerebrovascular events in patients with arterial hypertension and cardiovascular disease may have relation with direct effect of the infection or

by an unsuitable host reaction. Still case reports and the series shows the possibility of the chances cannot be refused [6].

**Table 1:** Summary of the neurological demonstration found in corona corona virus infections. In the first line it is the general findings of other corona viruses that infect humans and in the second line it is the specific findings of SARS-CoV-2, responsible for COVID-19

NEUROLOGICAL FINDINGS IN HUMAN CORONAVIRUS INFECTION		
PATHOGENS	CLINICAL MANIFESTATIONS	BIBLIOGRAPHY
1. Coronavirus (HCoV-229E, HCoV-OC43, SARS-CoV and HCoV-OC43)	<ul style="list-style-type: none"> <li><b>Acute:</b> Febrile seizures; Convulsions; Loss of consciousness; Ataxia; Anosmia or Hyposmia; Encephalomyelitis; Encephalitis; Myelitis; Neuritis. Acute Disseminated Encephalomyelitis (ADEM).</li> <li><b>Chronic:</b> myalgia, mood, and sleep disorders.</li> </ul>	Bohmwald et al. 2018; Hwang C, 2006; Ann Yeh E, et al. 2003.
2. COVID-19 (SARS-CoV-2)	<ul style="list-style-type: none"> <li><b>CNS:</b> headache, dizziness, impaired consciousness, ataxia, acute cerebrovascular disease, and epilepsy.</li> <li><b>PNS:</b> hypogeusia, anosmia or hyposmia, and neuralgia, mainly.</li> <li><b>Muscle injury</b></li> </ul>	Mao L., et al. 2020 Lechien J, et al. 2020
	Encephalopathy with <sup>1,3</sup> and without <sup>2</sup> evidence of the virus in the CNS	1. Zhou L, et al. 2020 2. Filatov, A. et al 2020 3. Moriguchi T, et al. 2020
	Guillain-Barré syndrome	Zhao H, et al. 2020

**Related Viral Infections and Common Neurological Complications**

Corona virus is not only the virus that is correlated with neurological complications. The recent outbreak due the Zika virus caused consequential neurological complications which includes microcephaly, Gullian- barre syndrome (GBS) and eye infections [7].

In 2009 H1N1 orthomyxovirus affected all the countries in 5 continents and most of the cases were reported in North and South America and the most affected age groups were the children and the young adults [8].

From the filovirus family, Ebolavirus caused severe hemorrhagic fever with remarkable epidemic capability and the fatality rate was also high. The outbreak was in 2013-2013 in West Africa was larger when compared to the other outbreaks, with 28,646 cases reported and 11,323 people succumbing. It followed its uniqueness in its geographical distribution and the country spread [9]. The hiding site of the ebolavirus is the CNS and during the recovery period it is responsible for relapses [10].

Several non-polio enteroviruses have aroused in recent years as a severe public health concerns, which includes EV-A71, caused epidemics of hand-foot and- mouth disease(HFMD) in South East Asia and EV-D68, caused a large outbreak of severe lower respiratory tract disease in North America [11].

**Neurological Disorders of Other Corona Virus**

Severe acute respiratory syndrome(SARS) which is known to be a zoonatic respiratory disease caused by the corona virus(SARS-CoV) which started in South East Asia and started spreading to other countries in 2003. Polyneuropathy, encephalitis, and aortic ischemic stroke is induced by the SARS-CoV [12]. The signs of the cerebral edema and meningeal vasodilatation can be detected in most cases of SARS which is demonstrated through the autopsy. The Middle East respiratory syndrome (MERS) in 2012 introduced MERS-CoV is another high pathogenic corona virus that has been introduced into the human population. The potentially neuroinvasive MERS-CoV 25.7% of the patients developed insanity and 8.6% experienced seizures [13].

**Hypothetical Findings or Relevant Neurological Complications**

The high prevalence of GBS after the swine flu vaccination hoist many claims that the vaccine was the cause of several other infectious diseases including postvaccinal encephalopathy, myelopathy and peripheral nerve lesions [14]. By these reports the US government asked to Leonard T Kurland, he is an neuroepidemiologist from the mayo clinic in Rochester, he provides reference data on the several incidence of a number of infectious diseases and neurological diseases including encephalitis and aseptic meningitis [15]. These experience gives a background for correct findings of the measure of risk present in association between the COVID-19 and a other neurological disease.

**Comparison between Direct Viral Effects and Adverse Effects of Vaccines Regarding Neurological Complications**

After the swine flu vaccination in the USA in 1976 a notable incidence of GBS took place, led to a debate on the possible linkage between influenza vaccinations and GBS [16]. The relative risk reported was 7.6 corresponding to about ten excess cases of GBS per million vaccinations. Several studies were conducted between 1978 and 2009 on the connection between influenza vaccination and GBS capitulated conflicting the results [17]. In Italy a case control study was managed between October 2010 and may 2011 and it was done to survey the connections between the influenza vaccination and GBS [17]. The relative risk of influenza vaccine and GBS is 2.1(95% CI 1.1, 3.9), giving an accountable risk from 2 to 5 GBS cases per 1,000,000 vaccinations. The above mentioned findings were in custody with the results of eight studies conducted during the 2009-2010 influenza vaccine campaign with a monovalent A/H1N1 vaccine and it showed a best small increase of the risk [17]. These studies does not alter the risk benefit profile of the seasonal influenza vaccination, though it can grab the attention to the need to develop a vaccine with commending safety profile.

**Barriers in Finding the Acute Versus Chronic Complications along with Cause-Effect Relationship between the Virus**

The unanticipated signs and symptoms of the COVID-19 pandemic led the health care community and the people around to react in different methods and to initiate different disagreement measures that impeded with a correct

assessment of the relation cause and its effect between the progress of symptoms, severity and complications of the disease and finally the outcome.

The measures includes, among others:

1. The varying control of the environment and places like transports, amusement parks, health care facility and work places)
2. The use of RT-PCR based assays in a uncontrolled manner on respiratory specimens because still some of them have no validity and reliability
3. There are many measures to introduce to decrease the social contacts.

These types of non standardized measures should be diverged with the intrinsic heterogeneity of viral infection and the reaction of the host, these includes:

1. The generative number
2. Span of the incubation period
3. Demographic characteristics of the patient
4. Clinical characteristics of the patient
5. The adverse effects of the treatment.

Through these measures the uprising of a neurological disease in the acute phase of the infection can be assessed by these approaches of this complex scenario, which is to be done to verify whether the disease is the direct effect of the viral aggression which includes, (meningitis, encephalitis) or an indirect immune-mediated effect.

### Prophylaxis and Treatments

The panic induced by the pandemic has major mirroring on many neurological disorders, and is based on the diagnostic evaluation and the management. The signs and symptoms that is recognized by the physicians or patients likely not requiring sudden neurological consultation have been delayed a early diagnosis and a actual treatment. The disordered management of the patients will lead to the risk for those who presented with a neurological indication of infection will face a negative effect for the prevention and the therapeutic outcome. Finally, the unrestricted use of the drugs before finishing proper clinical trials may lead the patients to unpredictable harm or adverse effects.

### Upcoming Management Ideas or Upcoming Directions

The available facts based on the neurological problems in people with COVID-19 is totally based on the clinical succession that is done only on a population base does not gives an clear picture or an idea, it only gives a wild guess. With this information we cannot forecast if this alliance ends with the intention of the outbreak, and mostly will be followed by many short and long term complications. The picture here will be further tangled because of the lack of knowledge of the variation of the infection, immunity duration, and the effects by the control measures<sup>[18]</sup>. As we studied, during the 1918 influenza pandemic and the unexpected pandemic COVID-19 has an occurrence of post infectious neurological complications, and based on the present observations surveillance programs should be implemented and the detection of neurological disorders as epidemiological markers. The Institute of Health Metrics an Evaluation, site of the Global Burden of Disease (GBD) cooperate each other and has developed projections of resource utilization in response to the COVID-19 pandemic<sup>[19]</sup>. The estimates are based on carving the peak of death

rates and the usage of hospital in Wuhan, China where the virus was originated.

The studies or information that is learned from the current and the past effects of the pandemics on neurological problems and the global health need for strengthening health sector to get sure that the research development efforts are directing towards the existing needs. People suffering with neurological disorders may be at risk of having complications of the infection. These observations have considerations on the management of acute neurological conditions like stroke and chronic conditions like myasthenia gravis. The measures like social distancing and limited visit to hospitals have produced many problems in the clinical care of the neurological conditions.

### Conclusion

Even though, the pandemic COVID-19 is mostly affected in the lungs and caused pneumonia man reports and studies indicates that the patients may also show other symptoms. In this we talk about the CNS complications of the patients, and they may develop olfactory and taste loss. This concludes that COVID-19 is not only affecting the respiratory tract and can cause in the nervous system.

The restraining impacts of the future epidemics requires long term investments in the health care sector and best collaboration between the international organizations, and methods to detect, treat and prevent future pandemics.

### Conflict of Interest

The authors declared no conflict of interest with respect to the authorship, research or publication of the article.

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