



COVID-19: A new highway for neurodegenerative diseases

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ABSTRACT

It is not very often seen that a pandemic leading towards an epidemic, but here we are discussing about how COVID-19 has the potential to trigger neurological disorders. Fascinating evidences demonstrated that COVID-19 infection is capable of modifying spectrum of clinical firm where neurological diseases are manifested due to the infection and also are responsible for the development of long termed diseases. In this review we will study how there is latent relationship between COVID-19 and neurological disorders like Parkinson's disease (PD), Alzheimer's (AD) and multiple sclerosis (MS). Specifically, in multiple sclerosis more than age, neuroimmunology related factors influence the cause of this disease. Various studies have shown association between neurological disorders and COVID-19. The important viewpoint here is to understand the SARS-CoV-2 causing infection which leads to development of COVID-19 affecting neuro balance.

Keywords: Covid-19, Neurological Disorders, Alzheimer's Disorder, Parkinson Disease, Sars-Cov-2, After-Effects of Covid-19

1. NEURODEGENERATIVE DISEASES

Neurodegenerative is a state when peripheral nervous system loses its function over time or when nerve cells undergoes loss of functioning or apoptosis¹. Currently there are many available treatments that help in reducing either mental or physical symptoms that are correlating with neurological diseases. However, there are no solid treatments to reduce the progression of the diseases or cure it, which is why researchers are studying this aspect in detail. Neurodegenerative diseases can be expected more towards individuals with increased/increasing age. Risks are higher for aged people. Currently the death date has reduced when compared to previous decade due to the improving technology in this world of medicine, however, this indicates the increased number of old people who are more susceptible to undergo some sort of neurodegenerative disorders². These types of situations demand for widening our understanding towards how neurological diseases work and how can we approach its prevention and treatment.

There are millions who undergo some or the other type of neurodegenerative diseases worldwide, the most common among them are Alzheimer's and Parkinson's disease. There is a statistical rise of registered neurodegenerative diseases since 2016³. It is stated that in western part of the globe there are about 930,000 people estimated to be active with Parkinson's diseases in the year 2020⁴. It is seen via different researches that along with an individual's gene the environmental factors contribute equally for development of any neurodegenerative disorder. Epigenetics is a widely studied subject in research and that can be a major contributing factor for the current issue. For instance, an individual might carry a gene which would have make them susceptible to certain disorder, but the trigger for the occurrence of the same depends on environmental exposure through the lifetime.

Similarly, in the case of COVID-19 pandemic, it initiated sequential after effect of neurodegenerative diseases and symptoms. Studies are still being carried out in order to understand how SARS-CoV-2 virus is capable of invading the brain and central nervous system⁵. In one of the studies Prof. Kevin Barnham suggests a possible approach of virus insulting brain cells followed by neurodegenerative disorders. We will look into its phenotypic and biochemical approach further.

2. COVID-19

Current WHO reports reveal a total number of 1,954,336 confirmed deaths. As we know it by now that COVID-19 is a contagious and acute disease. This was first noticed in Wuhan, China. It was in the year 2019 December that it was identified and had begun spreading worldwide ultimately leading to pandemic⁶. It was seen that individuals with fatigue, cough, fever, loss of smell/taste and breathing difficulty were tested positive for COVID 19 and later these symptoms were declared in order to detect the spread of disease. Within no time doctors found out that the symptoms are visible only after 14 days of viral exposure. Due to COVID-19, a group of people developed acute respiratory distress syndrome, which is hastened by cytokine storms, blood clots and septic shock. Due to heavy doses of medication severe damage has been observed in organs like lungs and heart⁷. COVID-19 is caused due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) when in close contact⁸. This spreads via aerosols and small droplets which consist of this virus and can spread anywhere leading to contamination of surfaces⁹. There are not many methods developed

to diagnose COVID-19 but currently the most accurate diagnosis is done using real time reverse transcription polymerase chain reaction (rRT-PCR)¹⁰. Government from every country had taken preventive measures in order to control the pandemic by executing law that involves maintenance of physical and social distancing along with quarantine rules and use of face masks.

Generally, outside the human as a host this particular virus is irradiated by household sanitizer/soap as it's protective gear is destroyed. Genetic analysis has proven that coronavirus has the ability to genetically cluster along with *Betacoronavirus* in lineage B which are all found as derivatives of bat strains¹¹. They are all interrelated as they show about 96% of undistinguishable characteristics. In this study we will further look into how does COVID-19 gives rise to sequel of neurodegenerative diseases. Coronavirus has changed the phase of medicine and research, there are many researches trying to understand its phenotype and mechanism.

2.1 How does COVID-19 trigger neurodegenerative diseases?

Several evidences show relation between latest cases of neurological disorders and COVID-19¹². People have experienced stroke, encephalopathy and polyneuritis post COVID-19 which is why scientists are showing keen interest in understanding the concept behind this situation. In one of the articles, it was reported that a woman in her mid-50's was tested positive for COVID-19 and after her recovery, she started seeing monkeys and lions in her own house. Not only hallucinations but also aggressiveness and disorientation were observed. Upon various check-ups it was interesting to see that the women had no psychiatric history plus she has crossed the age where she would develop psychosis. This was the first registered case that presented post COVID-19 trauma in this aspect¹³.

Some people at the hospital with COVID-19 definitely experienced agitation, confusion and disorientation. One of the reports focused on an individual who developed inflammation on brain tissues and undergone swelling. There was another report describing a patient's brain condition where the myelin is undergoing deterioration and is not reversibly destroyed in certain disorders such as MS. Sir Alysson Muotri says "The neurological symptoms are only becoming more and more scary." These symptoms may lead to life long problems¹⁴.

Researchers are still studying this aspect in order to get the basic doubts right. For example, what kind of people are at risk, is it only old people or young people are prone to this too? And the most important one being, what is the cause for all this symptom? It is suggested that this might be an outcome of overstimulation of the immune system, which is why the mechanism of the disease is very important. There was a study carried out by Michael and his colleagues, where they gathered clinical details of 125 people in the UK who fought COVID-19 and about 62% of them went through destroyed brain's blood supply like haemorrhages and 32 were going through altered mental stress, and ten among them experienced psychosis¹⁴.

It is yet to be studied about the uniqueness of these neurological after effects. Several neuroscientists were in dilemma if this was caused due to infection via the virus or some sort of inflammation. The pattern seen in almost all the patients has been pretty constant but the underlying mechanism is to be studied in detail. Once this query is solved clinicians could suggest the correct treatments and medicines to affected patients. because, without understanding the problem the whole treatment could be misleading and turn the situation haywire. It was agreed between many scientists that it is challenging to find this virus in the brain than in any other organ of the body¹³. Current diagnosis is done via the polymerase chain reaction and it is not successful enough to detect these viruses in the brain even after being highly sensitive. Cerebrospinal fluid surrounding the brain and spinal cord also fails to highlight presence of the virus. Researchers suggest that the possible explanation for this could be that the ACE2 receptor via which virus enters the human cell is not widely expressed in the brain cells as it is a protein. Getting virus through your central nervous system is very rare and this infection needs to be given priority based on the current situation.

SARS-CoV2 when enters a host causes various cascade of biochemical reactions. Similar situation is created when brain is considered, as SARS-CoV2 is affecting the nervous system and triggering PD¹⁵. When this virus enters the brain cells, they successfully impair all the cell organelles one by one, these organelles that are damaged increases the level of reactive oxygen species (intracellular). This in return leads to aggregation and misfolding of the proteins, which is the key reason in developing pathogenesis that leads to PD. Moreover, in further stages when virus hypes the angiotensin 2 level it indorses degradation of the brain. Mitochondria in a cell plays an important role in pathogenesis of PD as they are involved in the genetic expressions, therefore, upon mitochondrial downregulation due to the viral invasion it kicks-starts PD¹⁶.

The death rates have gown down due to the emerging technology, therefore, we have many aged people in our society which is why dementia has become very common among old people¹⁷. The current situation of COVID-19 pandemic has brought up some concern in regards to this. There seems to be some correlation between COVID-19 and dementia which is to be studied in detail and investigated properly¹⁸. Upon vigorous collection of data, it was seen that in the advanced stage of COVID-19 patients undergo dementia leading towards Alzheimer's disease without considering age as a factor. It is yet to be clinically proven if there is any correlation between these two aspects¹⁹. However, old patients who overcame COVID-19 have shown some symptoms of AD and MS. Individuals with COVID-19 are vulnerable to develop progressive symptoms of MS along with other neuropsychiatric problems. There are no specific evidences that support the relation between MS and neurodegeneration in Men. This can open new possibilities of research in relation with the sex of the patient²⁰.

Studies are yet to be carried out in major parts of the globe and researchers are succeeding in understanding the phenotypic as well genotypic possibilities of COVID-19 in relation with the neurodegenerative disorders.

3. CONCLUSION

In the recent history of public health, COVID-19 pandemic has been the most lethal and wide spread pandemic. It is just a matter of time when researchers will figure out if there is any long-term effect of COVID-19. Several studies suggested that there is no escape from infection effecting the nervous system, which is why this is going to be the major focus of the research industry.

It is very clearly known that SARS-CoV2 is responsible for cytokine storm that directly effects on the central nervous system and can lead to unmeasurable penalties. These effects can be effective either ways. COVID-19 having a sequel of neurodegenerative disorders like Alzheimer's disease, Parkinson Disease and Multiple Sclerosis are proven positive due to stressed molecular mechanism.

It is suggested that patients who endured COVID-19 should consider going for psychiatric and cognitive follow-ups. Primarily because if this persists it can lead to neuroinflammatory dysregulation causing PICS.

One must not take this pandemic just as a respiratory problem and not neurological issue. In fact, COVID-19 has a direct impact on the central nervous system and brain cells. Various studies should also be carried out in order to know how age can be a factor in understanding the mechanism of neurological issues in relation with the pandemic.

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