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A Systematic Review about Covid-19 Sequalae and Syndrome

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ABSTRACT

A new type of coronavirus (severe acute respiratory syndrome coronavirus 2; SARS-CoV-2) that has began in Wuhan, China in late 2019 has grasped the whole world. Since then, there are approximately 2.59 million deaths has been caused by Covid-19. After numerous attempts and hard work from healthcare system, this deadly virus is in control by using vaccines like Covaxin and Covishield. But new problems are emerging even after the discovery of vaccines. Patients have been experiencing various health problems after recovering from Covid-19. This review article discussed about different sequalae and syndromes that are emerging in patients after postcovid recovery.

Keywords: Covid-19, Sequalae, Syndrome, Postrecovery symptoms.

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INTRODUCTION

As of March 6, 2021, around 2.59 million fatalities and 65.8 million recoveries from coronavirus disease 2019 (COVID-19) have been reported around the globe. The COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was initially described as causing a severe acute respiratory syndrome. Clinical studies have since shown that COVID-19 is a systemic illness with the potential for multi organ complications. As the pandemic unfortunately continues, COVID-19 has the potential for a broader and more insidious effect, including the loss of skilled health-care personnel to post-COVID-19 disabilities.

There is a lot that we still don't understand about COVID-19, the disease caused by the SARS-CoV-2 virus that started in Wuhan, China, in 2019 and turned into a worldwide pandemic. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the third novel coronavirus identified in the last 18 years to have cross-species transmission^{1,2}. The vast number of decrease in fatalities are seen in patient due to discovery of vaccines like Bharat Biotech Covaxin and Oxford-AstraZeneca Covishield. The number of COVID-19 survivors being discharged from the hospital is increasing every day; however, to date, very little evidence is available on the long-term effects of COVID-19 faced by survivors following hospital discharge. However, the current literature focused on the post recovery syndrome and sequale of COVID-19.

Symptoms:

Originally, the most common symptoms of COVID-19 included:

- Fever
- Cough
- Shortness of breath

Doctors had expanded this list including these possible indication³:

- Muscle or body aches
- Headache
- Fatigue
- Loss of taste (ageusia)
- Loss of smell (anosmia)
- Sore throat
- Congestion or runny nose
- Nausea or vomiting
- Diarrhoea

These symptoms typically appear 2 to 14 days after exposure to the virus⁴, according to the U.S. Centers for Disease Control and Prevention (CDC). The duration of symptoms can be up to two weeks for mild cases and up to six weeks or more for severe cases⁵. What is becoming apparent, however, is that some patients may also experience coronavirus sequelae, or lasting complications that continue far beyond this time frame.

Late sequelae and syndrome:

Sequelae is a term used to describe the aftereffect of a disease, condition, or injury. Any viral infection can cause post-viral syndrome, which involves lingering symptoms (or sequelae) long after you fight off an infection. What those symptoms are—and if you'll experience them at all—can vary, and may depend on risk factors or your body's immune response.

For example, after the severe acute respiratory syndrome (SARS) outbreak of 2002-2003, one study found that people who were infected with the virus reported feeling fatigue, muscle weakness, and sleeping problems up to three years later. Early evidence indicates that similar symptoms could stick around for some COVID-19 patients as well⁶.

Though there is limited information on late sequelae of COVID-19, reports of persistent symptoms in persons who recovered from acute COVID-19 illness have emerged⁷. More serious complications appear to be less common but have been reported. These complications include:

- Cardiovascular: myocardial inflammation, ventricular dysfunction⁸
- Respiratory: pulmonary function abnormalities⁹
- Renal: acute kidney injury¹⁰
- Dermatologic: rash, alopecia¹¹
- Neurological: olfactory and gustatory dysfunction, sleep dysregulation, altered cognition, memory impairment¹²
- Psychiatric: depression, anxiety, changes in mood¹³

The NICE guideline scope published on 30 October 2020 defines post-COVID syndrome as signs and symptoms that develop during or following an infection consistent with COVID-19 which continue for more than 12 weeks and are not explained by an alternative diagnosis. The definition says the condition usually presents with clusters of symptoms, often overlapping, which may change over time and can affect any system within the body. It also notes that many people with post-COVID syndrome can also experience generalized pain, fatigue, persisting high temperature and psychiatric problems¹⁴.

If you have COVID-19, the illness that comes from infection with the recently discovered coronavirus, your symptoms may be relatively mild and manageable at home. That's true for most

people. But if you're older or have another illness such as diabetes or heart disease, you're more at risk for the serious form of COVID-19.

Some people -- about 1 in 6 -- will have complications, including some that are life-threatening. Many of these complications may be caused by a condition known as cytokine release syndrome or a cytokine storm. This is when an infection triggers your immune system to flood your bloodstream with inflammatory proteins called cytokines. They can kill tissue and damage your organs, including your lungs, heart, and kidneys.

COVID-19 complications may include the following:

Acute Respiratory Failure:

When you have acute respiratory failure, your lungs might not pump enough oxygen into your blood or might not take enough carbon dioxide out. Both of these problems can happen at the same time. In one study of 68 Chinese people who died of COVID-19, acute respiratory failure was the leading cause of death.¹⁵

Pneumonia:

A spike in pneumonia cases was the first sign of the new coronavirus in China. When you have pneumonia, the air sacs in your lungs become inflamed, making it harder to breathe.

Scientists who have studied images of very ill COVID-19 patients' lungs found them filled with fluid, pus, and cell debris. In those cases, patients' bodies weren't able to transfer oxygen to the blood to keep their systems working properly.¹⁶

Acute Respiratory Distress Syndrome (ARDS):

Early in the outbreak of COVID-19 in China, acute respiratory distress syndrome (ARDS) was one of the most common complications. With ARDS, the lungs are so severely damaged that fluid begins to leak into them. As a result, the body has trouble getting oxygen into the bloodstream. You may need mechanical help to breathe -- such as a ventilator -- until your lungs recover.¹⁷

Acute Liver Injury:

Research shows that the most seriously ill patients run the greatest risk of liver damage. Scientists aren't sure yet whether the virus harms the liver or if it happens for another reason. Acute liver injury and liver failure are life-threatening complications.¹⁸

Acute Cardiac Injury:

Studies of people in China who were hospitalized with COVID-19 found that some developed heart problems, including arrhythmias. Researchers studying people in Washington state who were very ill from COVID-19 and being treated in a hospital also found high levels of cardiac ailments. But it's not clear whether the virus itself affected patients' hearts, or if the damage happened simply because the illness caused such stress on their bodies overall. COVID-19 also could cause

cardiac problems that last long after people have recovered from the coronavirus infection. But since the illness is so new, that's not clear yet.

Secondary Infection:

A secondary infection means that you get an infection unrelated to the first problem you had. In this case, it means someone with COVID-19 gets infected with something else. A review of several studies done so far on hospitalized COVID-19 patients found that secondary infection is a possible -- but not common -- complication. Sometimes, a person fighting off, or recovering from, a virus gets infected by bacteria. Strep and staph are common culprits. This can be serious enough to raise the risk of death.

Acute Kidney Injury:

This doesn't seem to be a common complication, but if it happens, it's serious. If your kidneys stop working properly, doctors will start treatment to stop the damage. You might get dialysis (in which a machine filters your blood) until your kidneys get back to working normally. But sometimes, the damage doesn't heal and people get chronic kidney disease, which would need to be managed long term.

Septic Shock:

Sepsis happens when your body's reaction to an infection misfires. The chemicals released into your bloodstream to battle the illness don't trigger the right response, and instead your organs are damaged. If the process isn't stopped, you can go into what's called septic shock. If your blood pressure drops too much, septic shock can be fatal. Septic shock affected some people with COVID-19 in China¹⁹.

Disseminated Intravascular Coagulation:

When you have disseminated intravascular coagulation, or DIC, the body's blood-clotting response doesn't work right. Abnormal clots form, which can lead to internal bleeding or organ failure. In one study of Chinese COVID-19 patients, DIC was common among those who died.²⁰

Blood Clots:

A condition called disseminated intravascular coagulation (DIC) causes your body's blood-clotting response to work differently than it should. Unusual clots form, which can lead to internal bleeding or organ failure. In one study of Chinese COVID-19 patients, DIC was common among those who died.

A Dutch study found that nearly a third of people who were in the intensive care unit (ICU) for COVID-19 had blood clots. Some were in patients' legs (deep vein thrombosis or DVT), lungs (pulmonary embolism or PE), or arteries. But none of the patients had DIC. Some researchers say the coronavirus may be causing a new clotting condition, COVID-19-associated coagulopathy

(CAC). It's marked by different protein levels in your blood than the ones caused by DIC.²¹

Multisystem Inflammatory Syndrome in Children:

Some children and teens have been hospitalized with a condition called multisystem inflammatory syndrome in children (MIS-C) or paediatric multisystem inflammatory syndrome (PMIS). Doctors are still learning about it, but they think it's linked to the new coronavirus. Symptoms include fever, belly pain, vomiting, diarrhoea, rash, headache, and confusion. They're similar to those of toxic shock syndrome or Kawasaki disease, which causes inflamed blood vessels in children.

Chronic Fatigue:

Some people who've had COVID-19 develop a condition similar to chronic fatigue syndrome. They may have a brain fog, severe fatigue, pain, trouble thinking, or dizziness.

Rhabdomyolysis:

This is an extremely rare condition, but it's one COVID-19 researchers are watching. In rhabdomyolysis, your muscles break down and tissue dies. As cells fall apart, a protein called myoglobin floods your bloodstream. If your kidneys can't flush it out of your blood quickly enough, it can overwhelm them and cause death.²²

Autophagy:

Given the causal interaction between autophagy and apoptosis, the possible role of SARS-CoV-2 between them seems more complicated. Autophagy and apoptosis occur in the fierce battle between the virus and the host. Infected host cells gather a large number of autophagosomes to activate autophagy-linked apoptosis, aiming to cut off the loop of virus replication²³. Although the relationship between SARS-CoV-2 and autophagy currently remains unclear, possible mutually beneficial interactions cannot be completely ruled out²⁴. However, as the infection continues and the number of autophagosomes increases, the virus turns to promoting the accelerated formation and aggregation of autophagosomes to activate the apoptotic program, thereby facilitating better apoptotic use of cell remnants as carriers to accelerate viral spread. Further studies on the role of apoptosis and autophagy in the pathogenesis may have implications for the development of treatments for acute and chronic neurological sequelae²⁵.

Neurodegenerative Diseases:

Neurodegenerative disease is an umbrella concept including a range of conditions that primarily affect the neurons in the human brain and is one of the key factors leading to the decline in quality of life. Whether SARS-CoV-2 causes neurodegenerative diseases or accelerates their premature occurrence is still unclear, and it is also difficult to draw conclusions within just a few months. However, the high expression of the ACE2 receptor in a wide range of sites in the brain not only provides an initial target for SARS-CoV-2 to cause acute brain damage, it may also be the basis for

later neurodegenerative changes²⁶. This possibility is supported by the findings from recent studies that showed the presence of functional inhibition of viral and nicotinic acetylcholine receptor complexes in the pathogenesis of SARS-CoV-2 infection²⁷.

Alzheimer Disease (AD):

In addition to age, there are many other important risk factors for Alzheimer disease (AD). Recently published studies have focused on the potential causal relationship between viral infections and AD. Given the identification of damage to the CNS by SARS-CoV-2, there is concern regarding its long-term effects on cognitive function²⁸. It is possible that further long-term studies will be required to identify the relationships among SARS-CoV-2 infection, AD, and other neurodegenerative sequelae. Neuroinflammatory responses, synaptic pruning, and neuronal loss are the structural basis of AD, and SARS-CoV-2 infection most likely accelerates these processes.²⁹

Parkinson Disease (PD):

Compared with AD, the potential CNS damage that is localized to the substantia nigra striatum that can result in Parkinson disease (PD) seems to be more limited. However, several recent studies have shown that patients with PD not only show motor dysfunction, their cognitive and memory functions are also severely impaired³⁰. Also, the pathogenesis of PD is associated with neuroinflammation, synaptic pruning, and neuron loss, sharing commonalities with AD³¹. However, in PD, different CNS sites are damaged, with different types of neurons being more severely affected. Currently, although there is no direct evidence that SARS-CoV-2 causes or accelerates PD, it should be noted that the wide expression of ACE2 at different areas in the CNS provides a molecular basis for SARS-CoV-2 to mediate or accelerate the occurrence of PD.

Multiple Sclerosis (MS):

Multiple sclerosis (MS) is associated with focal gray and white matter demyelination and diffuse neurodegeneration of the brain caused by inflammation³³. Current knowledge of the neurological changes caused by SARS-CoV-2 shows some similarities with those found in MS. First, the pro-inflammatory ‘cytokine storm’ caused by SARS-CoV-2 infection is the initiating factor of CNS neuro inflammatory damage³⁴. Second, SARS-CoV-2 can cause demyelination in the brain and spinal cord³⁵. A recently published case report showed that SARS-CoV-2 infection was associated with signs and symptoms similar to those of MS. Previous studies have shown an association between coronavirus infection and the onset of MS³⁶. If an association between SARS-CoV-2 infection and demyelinating neurological disease does exist, this will result in a therapeutic dilemma, as immunotherapy is used to treat these diseases, including MS³⁷. More long-term studies will be required to identify the relationship between SARS-CoV-2 infection and MS.

CONCLUSION:

This article has discussed the various syndromes and sequelae that has been reported worldwide in patients after recovering from covid-19. Even though we got successful in defeating this virus but it still has impact in lives of patient. This article has concluded that we need more advanced treatment system that will prevent this various syndrome and helps to make patients life better.

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